ATT: Barb O'Bryen

28545

Access DB# _____

SEARCH REQUEST FORM

Scientific and Technical Information Center

NOV - 3 2000

Requester's Full Name: Dwayne C. Jones Examiner #: _____ Date: 03 NOV 00

Art Unit: 1614 Phone Number 308-4634 Serial Number: 09/287,377

Mail Box and Bldg/Room Location: 2007/CM1 Results Format Preferred (circle): PAPER DISK E-MAIL

2001: CM1

If more than one search is submitted, please prioritize searches in order of need.

****

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: see attached sheet.

Inventors (please provide full names): _____

Earliest Priority Filing Date: 11/05/1996

**For Sequence Searches Only* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.*

Please search claims 1, 3 and 14.

NOTE: Here are elected species for claims 3, 5, 7, 9 and 12. see attached sheet.

Point of Contact:
Barb O'Bryen
Technical Info. Specialist
CM1 12C14 Tel: 308-4291

****

STAFF USE ONLY	Type of Search		Vendors and cost where applicable	
Searcher:	JOE	NA Sequence (#)		STN 3.88
Searcher Phone #:		AA Sequence (#)		Dialog
Searcher Location:		Structure (#)	4	Questel/Orbit
Date Searcher Picked Up:		Bibliographic	X	Dr.Link
Date Completed:	11-29-00	Litigation		Lexis/Nexis
Searcher Prep & Review Time:	33	Fulltext		Sequence Systems
Clerical Prep Time:		Patent Family		WWW/Internet
Online Time:	67	Other		Other (specify)

PTO-1590 (1-2000)

=> fil reg; d stat que l19; fil capl; d que nos l33; fil medl; d que l53; d que l62; d que l67; d que l69; s l53 or l67 or l69

FILE 'REGISTRY' ENTERED AT 11:52:48 ON 29 NOV 2000
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

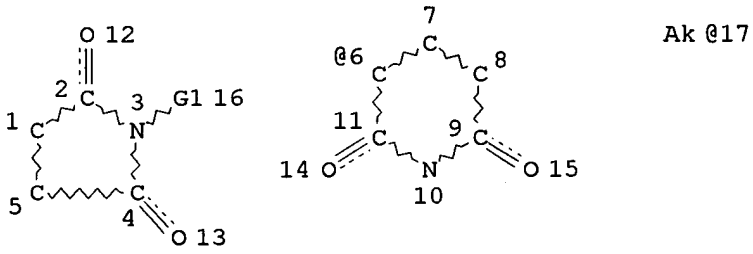
STRUCTURE FILE UPDATES: 28 NOV 2000 HIGHEST RN 304849-62-5
DICTIONARY FILE UPDATES: 28 NOV 2000 HIGHEST RN 304849-62-5

TSCA INFORMATION NOW CURRENT THROUGH July 8, 2000

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Structure search limits have been increased. See HELP SLIMIT for details.

L6 STR

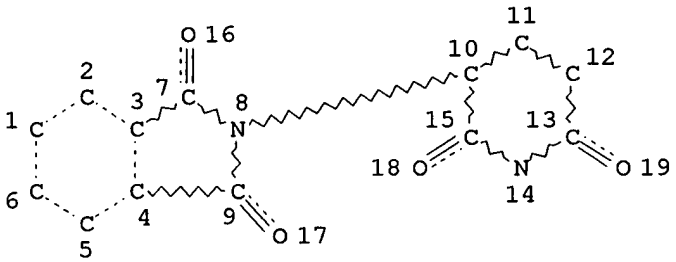


full fill search done on this structure

VAR G1=H/17/6
NODE ATTRIBUTES:
CONNECT IS E1 RC AT 17
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 17

STEREO ATTRIBUTES: NONE
L8 22307 SEA FILE=REGISTRY SSS FUL L6
L13 STR



subset search done looking for any of the following 3 structures

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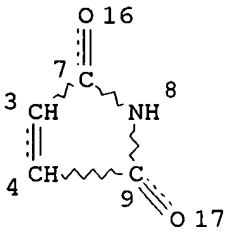
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I

NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE
L14 STR



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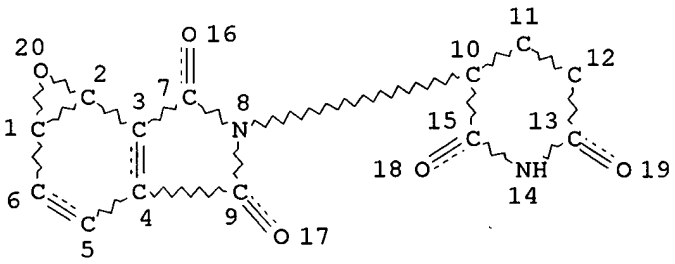
DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RING(S) ARE ISOLATED OR EMBEDDED
NUMBER OF NODES IS 7

STEREO ATTRIBUTES: NONE
L15 STR



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DEFAULT MLEVEL IS ATOM
DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:
RSPEC I
NUMBER OF NODES IS 20

STEREO ATTRIBUTES: NONE
L17 SCR 2043 – polymers
L19 339 SEA FILE=REGISTRY SUB=L8 SSS FUL (((L13 OR L14 OR L15)) NOT L17)

100.0% PROCESSED 20285 ITERATIONS 339 ANSWERS
SEARCH TIME: 00.00.03

FILE 'CAPLUS' ENTERED AT 11:52:50 ON 29 NOV 2000
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
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for records published or updated in Chemical Abstracts after December 26, 1996), unless otherwise indicated in the original publications.

FILE COVERS 1967 - 29 Nov 2000 VOL 133 ISS 23
FILE LAST UPDATED: 28 Nov 2000 (20001128/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

This file supports REG1stRY for direct browsing and searching of all substance data from the REGISTRY file. Enter HELP FIRST for more information.

Now you can extend your author, patent assignee, patent information, and title searches back to 1907. The records from 1907-1966 now have this searchable data in CAOLD. You now have electronic access to all of CA: 1907 to 1966 in CAOLD and 1967 to the present in CAPLUS on STN.

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L2        10026 SEA FILE=CAPLUS ABB=ON  ?ANGIOGEN?
L6              STR
L8        22307 SEA FILE=REGISTRY SSS FUL L6
L13             STR
L14             STR
L15             STR
L17             SCR 2043
L19         339 SEA FILE=REGISTRY SUB=L8 SSS FUL (((L13 OR L14 OR L15)) NOT
                L17)
L20        2217 SEA FILE=CAPLUS ABB=ON  L19
L21         895 SEA FILE=CAPLUS ABB=ON  ?THALIDOMIDE?
L22           1 SEA FILE=REGISTRY ABB=ON  HYDROCORTISONE/CN
L23           1 SEA FILE=REGISTRY ABB=ON  ACETAMINOPHEN/CN
L24       31169 SEA FILE=CAPLUS ABB=ON  L22 OR ?HYDROCORTISONE?
L25        9216 SEA FILE=CAPLUS ABB=ON  L23 OR ?ACETAMINOPHEN? OR TYLENOL
L26        3617 SEA FILE=CAPLUS ABB=ON  NONSTEROIDAL ANTI-INFLAMMATORY
                DRUGS/CT OR NSAID#
L28       51256 SEA FILE=CAPLUS ABB=ON  STEROID#/CW
L29       15477 SEA FILE=CAPLUS ABB=ON  ANTI INFLAMM?/OBI
L32         435 SEA FILE=CAPLUS ABB=ON  ANGIOSTA?
L33          25 SEA FILE=CAPLUS ABB=ON  (L20 OR L21 OR L24 OR L28) AND (L25 OR
                L26 OR L29) AND (L2 OR L32)
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FILE 'MEDLINE' ENTERED AT 11:52:50 ON 29 NOV 2000

FILE LAST UPDATED: 27 OCT 2000 (20001027/UP). FILE COVERS 1960 TO DATE.

MEDLINE thesauri in the /CN, /CT, and /MN fields incorporate the MeSH 2000 vocabulary. Enter HELP THESAURUS for details.

The OLDMEDLINE file segment now contains data from 1958 through 1965. Enter HELP CONTENT for details.

Left, right, and simultaneous left and right truncation are available in the Basic Index. See HELP SFIELDS for details.

THIS FILE CONTAINS CAS REGISTRY NUMBERS FOR EASY AND ACCURATE SUBSTANCE IDENTIFICATION.

```
L35       20452 SEA FILE=MEDLINE ABB=ON  ANGIOGENESIS INHIBITORS+NT/CT
```

Searched by Barb O'Bryen, STIC 308-4291

```
L36       86257 SEA FILE=MEDLINE ABB=ON  ANTI-INFLAMMATORY AGENTS, NON-STEROIDA
                L+NT/CT
L37      410405 SEA FILE=MEDLINE ABB=ON  D4.808./CT = Steroids
L38        7012 SEA FILE=MEDLINE ABB=ON  (L35 OR L37) AND L36
L48        8684 SEA FILE=MEDLINE ABB=ON  NEOVASCULARIZATION, PATHOLOGIC+NT/CT
L52         452 SEA FILE=MEDLINE ABB=ON  L48(L)DT/CT - DT - drug therapy
L53           4 SEA FILE=MEDLINE ABB=ON  L38 AND L52


L48        8684 SEA FILE=MEDLINE ABB=ON  NEOVASCULARIZATION, PATHOLOGIC+NT/CT
L54       39659 SEA FILE=MEDLINE ABB=ON  HYDROCORTISONE/CT
L55        1720 SEA FILE=MEDLINE ABB=ON  THALIDOMIDE/CT
L56        6933 SEA FILE=MEDLINE ABB=ON  ACETAMINOPHEN/CT
L57          23 SEA FILE=MEDLINE ABB=ON  (L54 OR L55) AND L56
L60       10256 SEA FILE=MEDLINE ABB=ON  ?ANGIOGEN? OR ANGIOSTA?
L62           0 SEA FILE=MEDLINE ABB=ON  (L48 OR L60) AND L57


L35       20452 SEA FILE=MEDLINE ABB=ON  ANGIOGENESIS INHIBITORS+NT/CT
L36       86257 SEA FILE=MEDLINE ABB=ON  ANTI-INFLAMMATORY AGENTS, NON-STEROIDA
                L+NT/CT
L37      410405 SEA FILE=MEDLINE ABB=ON  D4.808./CT
L38        7012 SEA FILE=MEDLINE ABB=ON  (L35 OR L37) AND L36
L39       60029 SEA FILE=MEDLINE ABB=ON  DRUG THERAPY, COMBINATION+NT/CT
L40       31710 SEA FILE=MEDLINE ABB=ON  DRUG COMBINATIONS+NT/CT
L48        8684 SEA FILE=MEDLINE ABB=ON  NEOVASCULARIZATION, PATHOLOGIC+NT/CT
L66       37024 SEA FILE=MEDLINE ABB=ON  DRUG SYNERGISM+NT/CT
L67           2 SEA FILE=MEDLINE ABB=ON  L38 AND (L39 OR L40 OR L66) AND L48


L35       20452 SEA FILE=MEDLINE ABB=ON  ANGIOGENESIS INHIBITORS+NT/CT
L36       86257 SEA FILE=MEDLINE ABB=ON  ANTI-INFLAMMATORY AGENTS, NON-STEROIDA
                L+NT/CT
L37      410405 SEA FILE=MEDLINE ABB=ON  D4.808./CT
L38        7012 SEA FILE=MEDLINE ABB=ON  (L35 OR L37) AND L36
L48        8684 SEA FILE=MEDLINE ABB=ON  NEOVASCULARIZATION, PATHOLOGIC+NT/CT
L68         619 SEA FILE=MEDLINE ABB=ON  L48(L)PC/CT - subheading PC = prevention & control
L69           4 SEA FILE=MEDLINE ABB=ON  L68 AND L38


L108         10 L53 OR L67 OR L69

=> fil embase; d que l81; d que l87; s l81 or l87; fil wpids; d que l99; fil drugu drugb;
d que l104

FILE 'EMBASE' ENTERED AT 11:53:25 ON 29 NOV 2000
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 FILE COVERS 1974 TO 27 Nov 2000 (20001127/ED)

 EMBASE has been reloaded. Enter HELP RLOAD for details.

 This file contains CAS Registry Numbers for easy and accurate
 substance identification.


L70        2952 SEA FILE=EMBASE ABB=ON  THALIDOMIDE/CT
L71       40293 SEA FILE=EMBASE ABB=ON  HYDROCORTISONE/CT
                    Searched by Barb O'Bryen, STIC  308-4291
```

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L72        19860 SEA FILE=EMBASE ABB=ON  PARACETAMOL/CT
L73         9023 SEA FILE=EMBASE ABB=ON  ANGIOGENESIS+NT/CT
L75       151830 SEA FILE=EMBASE ABB=ON  NONSTEROID ANTIINFLAMMATORY AGENT+NT/CT

L76       257783 SEA FILE=EMBASE ABB=ON  STEROID+NT/CT
L77         2697 SEA FILE=EMBASE ABB=ON  "NEOVASCULARIZATION (PATHOLOGY)"/CT
L80           43 SEA FILE=EMBASE ABB=ON  (L70 OR L71 OR L76) AND (L72 OR L75)
                 AND (L73 OR L77)
L81            8 SEA FILE=EMBASE ABB=ON  CB/CT AND L80



L70         2952 SEA FILE=EMBASE ABB=ON  THALIDOMIDE/CT
L71        40293 SEA FILE=EMBASE ABB=ON  HYDROCORTISONE/CT
L72        19860 SEA FILE=EMBASE ABB=ON  PARACETAMOL/CT = acetaminophen
L73         9023 SEA FILE=EMBASE ABB=ON  ANGIOGENESIS+NT/CT
L74          855 SEA FILE=EMBASE ABB=ON  ANGIOGENESIS INHIBITOR/CT
L75       151830 SEA FILE=EMBASE ABB=ON  NONSTEROID ANTIINFLAMMATORY AGENT+NT/CT

L76       257783 SEA FILE=EMBASE ABB=ON  STEROID+NT/CT
L77         2697 SEA FILE=EMBASE ABB=ON  "NEOVASCULARIZATION (PATHOLOGY)"/CT
L85         5692 SEA FILE=EMBASE ABB=ON  L73/MAJ OR L77/MAJ
L87           12 SEA FILE=EMBASE ABB=ON  (L70 OR L71 OR L76) AND (L72 OR L75)
                 AND L85 AND L74


L109          18 L81 OR L87


FILE 'WPIDS' ENTERED AT 11:53:28 ON 29 NOV 2000
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FILE LAST UPDATED: 28 NOV 2000              <20001128/UP>
>>>UPDATE WEEKS:
MOST RECENT DERWENT WEEK            200061   <200061/DW>
DERWENT WEEK FOR CHEMICAL CODING:   200061
DERWENT WEEK FOR POLYMER INDEXING:  200061
DERWENT WORLD PATENTS INDEX/ SUBSCRIBER FILE, COVERS 1963 TO DATE

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                                            SEE HELP COST <<<

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    RESOURCE, PLEASE VISIT
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>>> FOR DETAILS OF THE PATENTS COVERED IN CURRENT UPDATES,
    SEE http://www.derwent.com/covcodes.html  <<<


L88         1038 SEA FILE=WPIDS ABB=ON  HYDROCORTISONE OR HYDRO CORTISONE
L89        11429 SEA FILE=WPIDS ABB=ON  STEROID?
L90           58 SEA FILE=WPIDS ABB=ON  ?THALIDOMIDE?
L91          732 SEA FILE=WPIDS ABB=ON  ACETAMINOPHEN OR TYLENOL OR PARACETAMOL

L92         1689 SEA FILE=WPIDS ABB=ON  NONSTEROID? OR (NON(W)STEROID?)
L93          646 SEA FILE=WPIDS ABB=ON  NSAID#
L94         2134 SEA FILE=WPIDS ABB=ON  ?ANGIOGEN? OR ANGIOSTA?
L98          424 SEA FILE=WPIDS ABB=ON  NEOVASCULARI?
L99            8 SEA FILE=WPIDS ABB=ON  (L88 OR L89 OR L90) (10A)((L91 OR L92
                 OR L93)) (10A) (L94 OR L98)
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Searched by Barb O'Bryen, STIC 308-4291

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FILE 'DRUGU' ENTERED AT 11:53:29 ON 29 NOV 2000
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FILE 'DRUGB' ENTERED AT 11:53:29 ON 29 NOV 2000
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L100       15528 SEA ACETAMINOPHEN OR PARACETAMOL OR TYLENOL
L101       28853 SEA HYDROCORTISONE OR THALIDOMIDE
L102        7727 SEA ?ANGIOGEN?
L103         989 SEA ANTIANGIOGEN? OR ANGIOSTAT? OR NEOVASCULARI? OR ANTINEOVASC
                 ULAR?
L104           0 SEA L100 AND L101 AND (L102 OR L103)

=> dup rem l33,l108,l109,l99
FILE 'CAPLUS' ENTERED AT 11:53:58 ON 29 NOV 2000
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FILE 'MEDLINE' ENTERED AT 11:53:58 ON 29 NOV 2000

FILE 'EMBASE' ENTERED AT 11:53:58 ON 29 NOV 2000
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FILE 'WPIDS' ENTERED AT 11:53:58 ON 29 NOV 2000
COPYRIGHT (C) 2000 DERWENT INFORMATION LTD
PROCESSING COMPLETED FOR L33
PROCESSING COMPLETED FOR L108
PROCESSING COMPLETED FOR L109
PROCESSING COMPLETED FOR L99
L110          59 DUP REM L33 L108 L109 L99 (2 DUPLICATES REMOVED)
                 ANSWERS '1-25' FROM FILE CAPLUS
                 ANSWERS '26-34' FROM FILE MEDLINE
                 ANSWERS '35-52' FROM FILE EMBASE
                 ANSWERS '53-59' FROM FILE WPIDS

=> d ibib abs hitstr l110 1-25; d ibib ab l110 26-59; fil hom

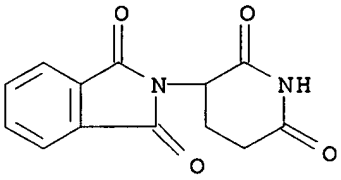

L110 ANSWER 1 OF 59  CAPLUS  COPYRIGHT 2000 ACS        DUPLICATE 1
ACCESSION NUMBER:         1999:68675  CAPLUS
DOCUMENT NUMBER:          130:291172
TITLE:                    Combination oral antiangiogenic therapy with
                          thalidomide and sulindac inhibits tumor growth
                          in rabbits
AUTHOR(S):                Verheul, H. M. W.; Panigrahy, D.; Yuan, J.; D'Amato,
                          R. J.
CORPORATE SOURCE:         Department of Surgery, Children's Hospital, Harvard
                          Medical School, Boston, MA, 02115, USA
SOURCE:                   Br. J. Cancer (1999), 79(1), 114-118
                          CODEN: BJCAAI; ISSN: 0007-0920
PUBLISHER:                Churchill Livingstone
DOCUMENT TYPE:            Journal
LANGUAGE:                 English
AB   Neovascularization facilitates tumor growth and metastasis formation.  In
     our lab., we attempt to identify clin. available oral efficacious drugs
                          Searched by Barb O'Bryen, STIC  308-4291
```

for **antiangiogenic** activity. Here, we report which non-steroidal anti-inflammatory drugs (**NSAIDs**) can inhibit corneal neovascularization, induced by basic fibroblast growth factor (bFGF) or vascular endothelial growth factor (VEGF). This **antiangiogenic** activity may contribute to the known effects of **NSAIDs** on gastric ulcers, polyps and tumors. We found that sulindac was one of the most potent **antiangiogenic NSAIDs**, inhibiting bFGF-induced neovascularization by 50% and VEGF-induced neovascularization by 55%. Previously, we reported that **thalidomide** inhibited growth factor-induced corneal neovascularization. When we combined sulindac with **thalidomide**, we found a significantly increased inhibition of bFGF- or VEGF-induced corneal neovascularization (by 63% or 74% resp.) compared with either agent alone ($P < 0.01$). Because of this strong **antiangiogenic** effect, we tested the oral combination of **thalidomide** and sulindac for its ability to inhibit the growth of V2 carcinoma in rabbits. Oral treatment of **thalidomide** or sulindac alone inhibited tumor growth by 55% and 35% resp. When given together, the growth of the V2 carcinoma was inhibited by 75%. Our results indicated that oral **antiangiogenic** combination therapy with **thalidomide** and sulindac may be a useful non-toxic treatment for cancer.

IT **50-35-1**, **Thalidomide**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(combination oral **antiangiogenic** therapy with **thalidomide** and sulindac inhibits tumor growth in rabbits)

RN 50-35-1 CAPLUS

CN 1H-Isoindole-1,3(2H)-dione, 2-(2,6-dioxo-3-piperidinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 42

REFERENCE(S):
(1) Bossi, P; Cancer Res 1995, V55, P5049 CAPLUS
(2) Chiu, C; Cancer Res 1997, V57, P4267 CAPLUS
(3) Duggan, D; J Pharm Exp Ther 1977, V201, P8 CAPLUS
(4) D'Amato, R; Proc Natl Acad Sci USA 1994, V91, P4082 CAPLUS
(7) Folkman, J; Ann Surg 1987, V206, P374 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 2 OF 59 CAPLUS COPYRIGHT 2000 ACS DUPLICATE 2
ACCESSION NUMBER: 1998:341491 CAPLUS
DOCUMENT NUMBER: 129:12742
TITLE: Methods and compositions using **thalidomide** or other **angiogenesis**-inhibitory compound and **anti-inflammatory** agent for inhibition of **angiogenesis**
INVENTOR(S): D'Amato, Robert J.
PATENT ASSIGNEE(S): Children's Medical Center, USA
SOURCE: PCT Int. Appl., 63 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
Searched by Barb O'Bryen, STIC 308-4291

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9819649	A2	19980514	WO 1997-US20116	19971104
WO 9819649	A3	19980625		
W:	AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM			
RW:	GH, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG			
AU 9851973	A1	19980529	AU 1998-51973	19971104
EP 963200	A2	19991215	EP 1997-946884	19971104
R:	AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI			
PRIORITY APPLN. INFO.:			US 1996-28708	19961105
			US 1997-963058	19971103
			WO 1997-US20116	19971104

OTHER SOURCE(S): MARPAT 129:12742

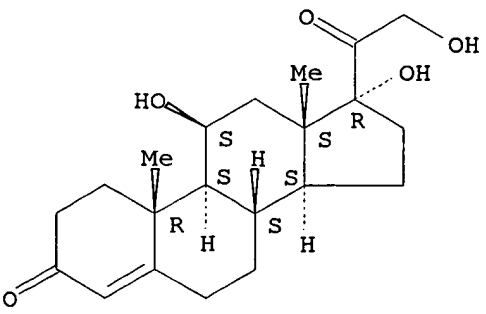
AB A group of compds. that effectively inhibit **angiogenesis** is provided. More specifically, **thalidomide** and various related compds.,e.g. **thalidomide** precursors, analogs, metabolites and hydrolysis products, have been shown to inhibit **angiogenesis** and to treat disease states resulting from **angiogenesis**. Addnl., antiinflammatory drugs, such as steroids and **NSAIDs** can inhibit **angiogenesis**-dependent diseases either alone or in combination with **thalidomide** and related compds. Importantly, these compds. can be administered orally.

IT **50-23-7**, Cortisol **50-35-1**, **Thalidomide**
50-35-1D, **Thalidomide**, metabolites and derivs.
103-90-2, **Acetaminophen 541-59-3**,
1H-Pyrrole-2,5-dione **158902-90-0 158908-13-5**
158923-53-6
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**thalidomide** or other **angiogenesis**-inhibitory compd. and **anti-inflammatory** agent for inhibition of **angiogenesis**)

RN 50-23-7 CAPLUS

CN Pregn-4-ene-3,20-dione, 11,17,21-trihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)

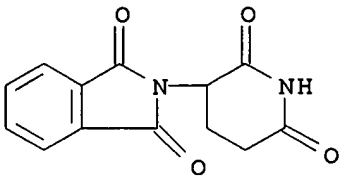
Absolute stereochemistry.



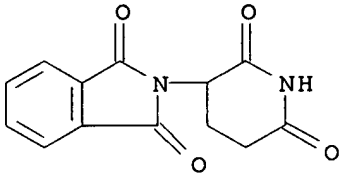
RN 50-35-1 CAPLUS

CN 1H-Isoindole-1,3(2H)-dione, 2-(2,6-dioxo-3-piperidinyl)- (9CI) (CA INDEX

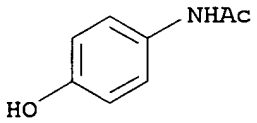
NAME)



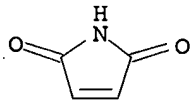
RN 50-35-1 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-(2,6-dioxo-3-piperidinyl)- (9CI) (CA INDEX NAME)



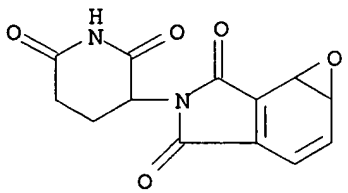
RN 103-90-2 CAPLUS
CN Acetamide, N-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)



RN 541-59-3 CAPLUS
CN 1H-Pyrrole-2,5-dione (9CI) (CA INDEX NAME)

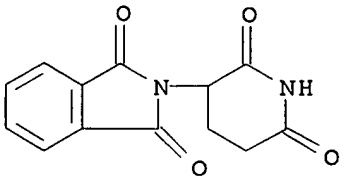


RN 158902-90-0 CAPLUS
CN 4H-Oxireno[e]isoindole-4,6(5H)-dione, 5-(2,6-dioxo-3-piperidinyl)-1a,6b-dihydro- (9CI) (CA INDEX NAME)



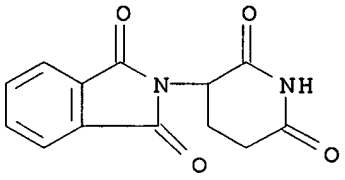
RN 158908-13-5 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-(2,6-dioxo-3-piperidinyl)dihydroxy- (9CI) (CA INDEX NAME)

Searched by Barb O'Bryen, STIC 308-4291



2 (D1—OH)

RN 158923-53-6 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-(2,6-dioxo-3-piperidinyl)hydroxy- (9CI) (CA INDEX NAME)



D1—OH

L110 ANSWER 3 OF 59 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:741947 CAPLUS
DOCUMENT NUMBER: 133:291146
TITLE: Novel uses of mammalian OX2 protein and related reagents
INVENTOR(S): Hoek, Robert M.; Sedgwick, Jonathan D.
PATENT ASSIGNEE(S): Schering Corporation, USA
SOURCE: PCT Int. Appl., 20 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000061171	A2	20001019	WO 2000-US9719	20000412
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LU, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, PT, RO, RU, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UZ, VN, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				

PRIORITY APPLN. INFO.: US 1999-290825 19990413

AB Compns. and methods for using mammalian ligand OX2 to treat an abnormal physiol. condition in an individual. The methods comprise administering a therapeutically effective amt. of OX2 alone, or in combination with other therapeutic reagents; or an OX2 antagonist.

Searched by Barb O'Bryen, STIC 308-4291

L110 ANSWER 4 OF 59 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:666590 CAPLUS
DOCUMENT NUMBER: 133:242678
TITLE: **Angiogenesis** inhibition with pharmaceutical containing reaction products of hyaluronic acid, CM-cellulose and carbodiimide
INVENTOR(S): Moulton, Steven
PATENT ASSIGNEE(S): Trustees of Boston University, USA
SOURCE: PCT Int. Appl., 28 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000054762	A2	20000921	WO 2000-US6819	20000315

W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-124703 19990315
AB **Angiogenesis** is inhibited by the local administration of a pharmaceutical prepn. formed from the reaction of hyaluronic acid, CM-cellulose and a carbodiimide. The prepn., which can be in the form of a film or a gel, is advantageously applied directly to the site of a tumor, such as a cancerous tumor, used in conjunction with other chemotherapeutic techniques, or used to treat a chronic inflammatory condition, such as rheumatoid arthritis, endometriosis, arteriosclerosis, intimal hyperplasia, proliferative retinopathy, and the like. Seprafilm inhibited the growth of vessels and the formation of adhesions in mice.

L110 ANSWER 5 OF 59 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:608944 CAPLUS
DOCUMENT NUMBER: 133:187931
TITLE: Gene sequence variations with utility in determining the treatment of disease
INVENTOR(S): Stanton, Vincent, Jr.
PATENT ASSIGNEE(S): Variagenics, Inc., USA
SOURCE: PCT Int. Appl., 2884 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000050639	A2	20000831	WO 2000-US1392	20000120

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

Searched by Barb O'Bryen, STIC 308-4291

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-121047 19990222
US 1999-139440 19990615
US 1999-357743 19990720

AB The present disclosure describes the use of genetic variance information for genes involved in gene pathways in the selection of effective methods of treatment of a disease or condition. The variance information is indicative of the expected response of a patient to a method of treatment. For some drugs, >90% of the measurable variation in selected pharmacokinetic parameters has been shown to be heritable. Methods of detg. relevant variance information and addnl. methods of using such variance information are also described. This invention addresses the difficulties that arise in treating the following disease categories: (1) neurol. and psychiatric disease; (2) pharmacokinetic and dynamic indexes including efficacy, absorption, distribution, metab., and excretion, as well as safety and toxicity parameters; (3) inflammation and immune disease; (4) endocrine and metabolic disease; (5) cardiovascular and renal disease; and (6) cancer. Further, the invention provides methods and compns. for identifying and predicting inter-patient differences in response to drugs in order to achieve superior efficacy and safety in selected patient populations. Extensive tables are provided that (1) list genes that may be involved in pharmacol. response to various diseases, (2) matrix tables showing the intersection of genes and therapeutic indications -- i.e., which categories of genes are most likely to account for interpatient variation in response to treatments for which diseases, (3) exemplary DNA sequence variances in genes relevant to the methods described, (4) lists of exemplary compds in clin. development for the various disease indications.

L110 ANSWER 6 OF 59 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:475502 CAPLUS
DOCUMENT NUMBER: 133:94539
TITLE: Composition and formulations and their use as nociceptic, anti-anxiolytic and anabolic agents
INVENTOR(S): Nyce, Jonathan W.
PATENT ASSIGNEE(S): USA
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000040172	A1	20000713	WO 2000-US180	20000105

W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM

RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1999-114773 19990105

AB Compn. and formulations comprising a first agent such as folinic acid, pharmaceutically acceptable salts thereof or mixts. thereof, and a second agent(s) such as analgesics, muscle relaxants, mood disorder agents, anti-inflammatories, anti-migraine agents, anti-emetics, diuretics, high

protein composites, and the like are claimed. The products are suitable as nociceptics and for the treatment of wasting disorders, bulimia, anorexia nervosa, anxiety, irritability and other symptoms assocd. with premenstrual syndrome, as well as for administration either in conjunction with steroids or to compensate adenosine depletion and/or bizarre behavior or aggression common in steroid users. Administration of dehydroepiandrosterone (300 mg/kg) or methyltestosterone (40 mg/kg) daily to rats for 2 wk showed multi-organ depletion of adenosine. Co-administration of folinic acid completely abrogated adenosine depletion. Folinic acid administered alone induced increase in adenosine levels for all organs studied.

REFERENCE COUNT: 1
REFERENCE(S): (1) Gaeta; US 5767278 A 1998 CAPLUS

L110 ANSWER 7 OF 59 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:456819 CAPLUS
DOCUMENT NUMBER: 133:84238
TITLE: 3-heteroarylidenyl-2-indolinone compounds for modulating protein kinase activity and for use in cancer chemotherapy
INVENTOR(S): Langecker, Peter J.; Shawver, Laura Kay; Tang, Peng Cho; Sun, Li
PATENT ASSIGNEE(S): Sugen, Inc., USA
SOURCE: PCT Int. Appl., 148 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000038519	A1	20000706	WO 1999-US31232	19991230

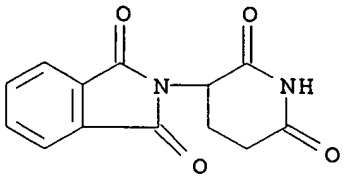
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 1998-114313 19981231
OTHER SOURCE(S): MARPAT 133:84238

AB 3-Heteroarylidenyl-2-indolinone compds. are provided that modulate the enzymic activity of protein kinases and therefore are expected to be useful in the prevention and treatment of protein kinase-related cellular disorders, e.g. cancer. Furthermore, these compds. are expected to enhance the efficacy of other chemotherapeutic agents, in particular, fluorinated pyrimidines, in the treatment of cancer.

IT **50-35-1, Thalidomide**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(heteroarylidenylindolinone derivs. for modulating protein kinase activity and in cancer chemotherapy)

RN 50-35-1 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-(2,6-dioxo-3-piperidinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 3
REFERENCE(S): (1) Sugen Inc; WO 9640116 A1 1996 CAPLUS
(2) Tang; US 5792783 A 1998 CAPLUS
(3) Tang; US 5886020 A 1999 CAPLUS

L110 ANSWER 8 OF 59 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:277810 CAPLUS
DOCUMENT NUMBER: 132:326056
TITLE: Systems for oral delivery
INVENTOR(S): Russell-Jones, Gregory John
PATENT ASSIGNEE(S): Biotech Australia Pty. Ltd., Australia
SOURCE: PCT Int. Appl., 32 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000022909	A2	20000427	WO 1999-IB1872	19991018
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 2000010712	A5	20000508	AU 2000-10712	19991018
PRIORITY APPLN. INFO.:			US 1998-104827	19981019
			WO 1999-IB1872	19991018

AB A pharmaceutical and a biol. active substance, for oral administration, can be "coated" or "encapsulated" with a carboxylic acid, such that the substance is protected from proteolysis in the stomach and is taken up from the intestine. It is thought that the carboxylic acids coat and protect the active agent from the proteolytic environment of the stomach, allowing the agent to pass safely through the stomach and to be absorbed in the small intestines. The carboxylic acid agent complex can be adopted for oral, nasal, buccal, and transdermal delivery of moderately sol. and even insol. bioactive agents.

L110 ANSWER 9 OF 59 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:53401 CAPLUS
DOCUMENT NUMBER: 132:88759
TITLE: Prophylactic treatment of neovascularization in macular degeneration using **anti-inflammatory** steroids
INVENTOR(S): Gillies, Mark Cedric; Penfold, Philip Leslie; Billson, Francis Alfred
PATENT ASSIGNEE(S): The University of Sydney, Australia
SOURCE: PCT Int. Appl., 14 pp.
Searched by Barb O'Bryen, STIC 308-4291

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000002564	A1	20000120	WO 1999-AU565	19990712
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9947632	A1	20000201	AU 1999-47632	19990712
PRIORITY APPLN. INFO.:			AU 1998-4607	19980710
			AU 1998-5847	19980911
			WO 1999-AU565	19990712

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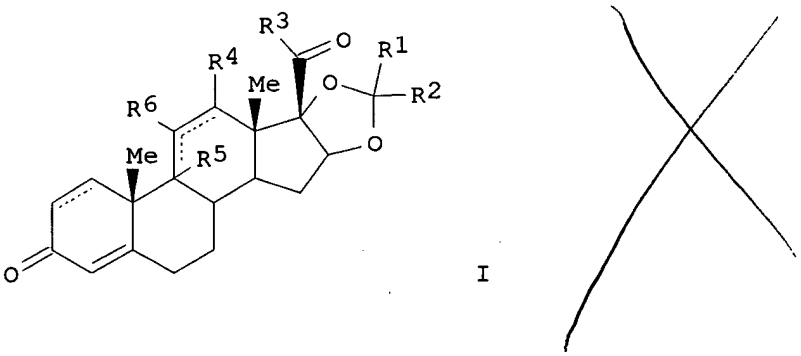


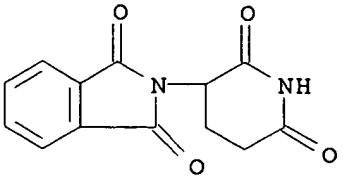
I

AB This invention relates to the prophylaxis of choroidal neovascularization in macular degeneration by the introduction of a suitable anti-inflammatory agent into the vitreous. In particular, it relates to the prophylaxis of neovascularization with an anti-inflammatory steroid, such as an 11-substituted 16.alpha.,17.alpha.-substituted methylenedioxy steroid of formula (I) wherein R1 and R2 are hydrogen or alkyl; -Ca-Cb- is -CH2-CH2-, -CH=CH-, -CH2CH(CH3)- or -CH=C(CH3)-; R3 is Me, hydroxymethyl or alkylcarbonyloxymethyl, methylaminoalkylenecarbonyloxymethyl, or phenylaminoalkylenecarbonyloxymethyl; R4 + R6 and R5 + R6 is epoxy; R5 is halogen; R6 is hydroxyl, keto, or alkanoyl. More particularly, it relates to prophylaxis with triamcinolone acetonide.

IT **50-35-1, Thalidomide**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prophylactic treatment of neovascularization in macular degeneration using **anti-inflammatory** steroids in combination with an **antiangiogenesis** agent)

RN 50-35-1 CAPLUS

CN 1H-Isoindole-1,3(2H)-dione, 2-(2,6-dioxo-3-piperidinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 4
REFERENCE(S): (1) Merck & Co Inc; AU 1972197 A 1997
(2) Merck & Co Inc; AU 5088498 A 1998
(3) The University Of Sydney; AU 7340694 A 1995
(4) Zander; WO 9829122 A 1998

L110 ANSWER 10 OF 59 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 2000:636163 CAPLUS
DOCUMENT NUMBER: 133:227868
TITLE: Supplemented and unsupplemented tissue sealants, method of their production and use
INVENTOR(S): Macphee, Martin James; Drohan, William Nash; Liau, Gene; Haudenschild, Christian
PATENT ASSIGNEE(S): The American National Red Cross, USA
SOURCE: U.S., 79 pp., Cont.-in-part of U.S. Ser. No. 351,006, abandoned.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 6
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6117425	A	20000912	US 1995-474086	19950607
AU 9884192	A1	19981105	AU 1998-84192	19980911
PRIORITY APPLN. INFO.:			US 1990-618419	19901127
			US 1991-798919	19911127
			US 1993-31164	19930312
			US 1994-328552	19941025
			US 1994-351006	19941207
			AU 1994-63648	19940314

AB This invention provides supplemented tissue sealants, methods for their prodn. and use thereof. Disclosed are tissue sealants supplemented with at least one cytotoxin or cell proliferation inhibiting compn. The compn. may be further supplemented with, for example, one or more antibodies, analgesics, anticoagulants, anti-inflammatory compds., antimicrobial compns., cytokines, drugs, growth factors, interferons, hormones, lipids, demineralized bone or bone morphogenetic proteins, cartilage inducing factors, oligonucleotides polymers, polysaccharides, polypeptides, protease inhibitors, vasoconstrictors or vasodilators, vitamins, minerals, stabilizers and the like. Heparin binding growth factor-1 (HBGF-1) was added at 10 .mu.g in a fibrinogen complex contg. heparin 10, thrombin 0.5 U/mL, and CaCl2 40 mM for testing the HBGF-1 diffusion from a fibrin glue clot.

REFERENCE COUNT: 61
REFERENCE(S): (6) Anon; DE 3037270 1982 CAPLUS
(12) Anon; WO 8600526 1986 CAPLUS
(13) Anon; WO 8601814 1986 CAPLUS
(14) Anon; WO 8603122 1986 CAPLUS
(16) Anon; EP 0312208 1988 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 11 OF 59 CAPLUS COPYRIGHT 2000 ACS
Searched by Barb O'Bryen, STIC 308-4291

ACCESSION NUMBER: 2000:10622 CAPLUS
DOCUMENT NUMBER: 132:31278
TITLE: **Angiostatic steroids**
INVENTOR(S): Clark, Abbot F.; Conrow, Raymond E.
PATENT ASSIGNEE(S): Alcon Laboratories, Inc., USA
SOURCE: U.S., 18 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6011023	A	20000104	US 1997-924419	19970827

AB Methods and compns. for preventing and treating neovascularization with **angiostatic** steroids is disclosed.
REFERENCE COUNT: 30
REFERENCE(S):
(1) Anon; WO 8702672 1987 CAPLUS
(2) Anon; WO 9103245 1991 CAPLUS
(3) Aristoff; US 4975537 1990 CAPLUS
(4) Ashino-Fuse; Int J Cancer 1989, V44, P859 CAPLUS
(5) BenEzra; Journal of Ophthalmology 1978, V86(4), P455 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 12 OF 59 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:795640 CAPLUS
DOCUMENT NUMBER: 132:44996
TITLE: Wound treatment through inhibition of adenosine diphosphate ribosyl transferase
INVENTOR(S): Leibovich, Samuel J.
PATENT ASSIGNEE(S): University of Medicine and Dentistry of New Jersey, USA
SOURCE: PCT Int. Appl., 65 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9963982	A1	19991216	WO 1999-US13264	19990611
W: AU, CA, JP				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9944383	A1	19991230	AU 1999-44383	19990611

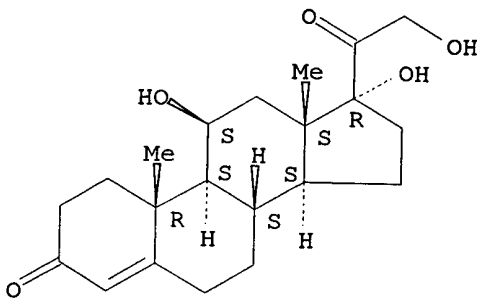
PRIORITY APPLN. INFO.: US 1998-88924 19980611
WO 1999-US13264 19990611

AB A method is disclosed for healing a wound in a mammal which comprises (A) providing a therapeutic wound healing compn. comprising a therapeutically effective amt. of an inhibitor of mono-ADP-ribosyl transferase to inhibit ADP-ribosylation of vascular endothelial growth factor, and (B) contacting the therapeutic wound healing compn. with a wound in a mammal. Also disclosed are wound healing compns. and methods for prepg. and using the wound healing compns. and the pharmaceutical products in which the therapeutic compns. may be used. Further disclosed are therapeutic dermatol.-wound healing compns. useful to minimize and treat diaper dermatitis and methods for prepg. and using the therapeutic dermatol.-wound healing compns.
IT **50-23-7, Hydrocortisone**

Searched by Barb O'Bryen, STIC 308-4291

RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ADP ribosyl transferase inhibitors and antiinflammatory agents for wound healing and diaper dermatitis)
RN 50-23-7 CAPLUS
CN Pregn-4-ene-3,20-dione, 11,17,21-trihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 1
REFERENCE(S): (1) Willward; US 4029770 A 1977 CAPLUS

L110 ANSWER 13 OF 59 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:184144 CAPLUS
DOCUMENT NUMBER: 130:232485
TITLE: Use of immunostimulatory oligonucleotides for preventing or reducing antigen-stimulated, granulocyte-mediated inflammation
INVENTOR(S): Ray, Eyal
PATENT ASSIGNEE(S): The Regents of the University of California, USA
SOURCE: PCT Int. Appl., 69 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9911275	A2	19990311	WO 1998-US18382	19980904
WO 9911275	A3	19990603		
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
AU 9893023	A1	19990322	AU 1998-93023	19980904
EP 1009413	A2	20000621	EP 1998-945877	19980904
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				

PRIORITY APPLN. INFO.: US 1997-927120 19970905
WO 1998-US18382 19980904

AB The invention relates to methods for preventing or reducing antigen-stimulated, granulocyte-mediated inflammation in tissue of an antigen-sensitized mammal host by delivering an immunostimulatory

oligonucleotide to the host. In addn., methods for using the immunostimulatory oligonucleotides to boost a mammal host's immune responsiveness to a sensitizing antigen (without immunization of the host by the antigen) and shifting the host's immune responsiveness to a Th1 phenotype to achieve various therapeutic ends are provided. Kits for practicing the methods of the invention are also provided.

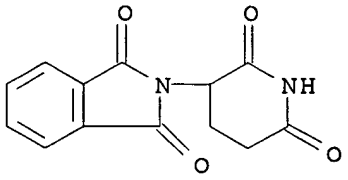
L110 ANSWER 14 OF 59 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:48631 CAPLUS
DOCUMENT NUMBER: 130:119599
TITLE: Pharmaceutical compositions comprising an **angiostatic** steroid combined with a hyaluronan for increasing neovascularization and **angiogenesis** during wound healing
INVENTOR(S): Seed, Michael P.; Alam, Chandan; Willoughby, Derek A.
PATENT ASSIGNEE(S): Hyal Pharmaceutical Corporation, Can.
SOURCE: PCT Int. Appl., 84 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9901142	A1	19990114	WO 1998-CA649	19980703
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2208916	AA	19990103	CA 1997-2208916	19970703
AU 9882021	A1	19990125	AU 1998-82021	19980703
PRIORITY APPLN. INFO.:			CA 1997-2208916	19970703
			WO 1998-CA649	19980703

AB A pharmaceutical compn. is disclosed for increasing neovascularization and **angiogenesis** during wound healing in a mammal beyond the level of neovascularization and **angiogenesis** which would occur at the wound site without any treatment, the compn. comprising an effective amt. of any **angiostatic** steroid which has reduced or no deteriorative or detrimental side effects, combined with an effective amt. of a form of hyaluronan, e.g. hyaluronic acid or a pharmaceutically acceptable salt thereof.
REFERENCE COUNT: 3
REFERENCE(S): (1) Okada, M; Endocr J (Tokyo) 1995, V42, P675 CAPLUS
(2) Union Carbide Chem Plastic; EP 0368253 A 1990
(3) Upjohn Co; WO 9015816 A 1990

L110 ANSWER 15 OF 59 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:760382 CAPLUS
DOCUMENT NUMBER: 132:73073
TITLE: **Thalidomide** as an emerging immunotherapeutic agent
AUTHOR(S): Marriott, J. B.; Muller, G.; Dalgleish, A. G.
CORPORATE SOURCE: Dept of Cellular and Molecular Sciences, Division of Oncology, St George's Hospital Medical School, London, UK
SOURCE: Immunol. Today (1999), 20(12), 538-540
CODEN: IMTOD8; ISSN: 0167-4919
Searched by Barb O'Bryen, STIC 308-4291

PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 52 refs. **Thalidomide** first hit the headlines with alarming reports of birth defects after pregnant women took the drug to combat morning sickness. Now, the drug has been shown to have important immunomodulatory and anti-inflammatory effects that may be useful in the treatment of AIDS and cancer.
IT **50-35-1, Thalidomide**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**thalidomide**: emerging immunotherapeutic)
RN 50-35-1 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-(2,6-dioxo-3-piperidinyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 52
REFERENCE(S): (1) Alexander, L; AIDS Res Hum Retroviruses 1997, V13, P301 CAPLUS
(3) Azuma, A; Biol Pharm Bull 1996, V19, P1001 CAPLUS
(4) Chen, T; Drug Metab Dispos 1989, V17, P402 CAPLUS
(5) Corral, L; Mol Med 1996, V2, P506 CAPLUS
(6) D'Amato, R; Proc Natl Acad Sci 1994, V91, P4082 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

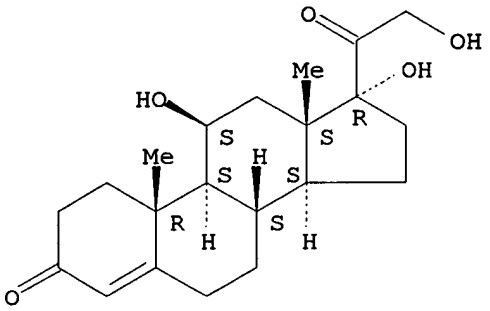
L110 ANSWER 16 OF 59 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1999:672339 CAPLUS
DOCUMENT NUMBER: 132:520
TITLE: **Angiostatic** activity of steroids in the chick embryo CAM and rabbit cornea models of neovascularization
AUTHOR(S): McNatt, Loretta G.; Weimer, Lori; Yanni, John; Clark, Abbot F.
CORPORATE SOURCE: Alcon Laboratories, Inc., Fort Worth, TX, USA
SOURCE: J. Ocul. Pharmacol. Ther. (1999), 15(5), 413-423
CODEN: JOPTFU; ISSN: 1080-7683
PUBLISHER: Mary Ann Liebert, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Ocular neovascular diseases represent a major cause of blindness in the world. **Angiostatic** steroids are a unique class of compds. which inhibit the formation of new blood vessels in various models, including ocular models of **angiogenesis**. In search of potent new anti-**angiogenic** agents for the treatment of ocular neovascular disease, a large group of steroids were evaluated for **angiostatic** activity in the chick embryo CAM model. **Angiostatic** activity was found among all steroid classes included in the study. There was a good correlation between the **angiostatic** efficacies of 15 diverse steroids tested in the chick CAM and in the rabbit LPS-induced corneal pocket models of neovascularization ($r=0.76$, $p=0.01$). These studies show that potent **angiostatic** steroids inhibit neovascularization in two different animal models, suggesting a common

mechanism of action. Glucocorticoid therapy is sometimes assocd. with ocular side effects. Two of the most potent **angiostatic** steroids, AL-3789 and AL-4940, were evaluated for glucocorticoid-mediated anti-inflammatory activity in the in vitro U937 cell model of LPS-induced IL-1 induction and found to be devoid of glucocorticoid activity. **Angiostatic** steroids which lack glucocorticoid activity should be attractive drug candidates for treating ocular neovascular disease.

IT **50-23-7**, Cortisol
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**angiostatic** activity of steroids in chick embryo CAM and rabbit cornea models of neovascularization)

RN 50-23-7 CAPLUS
CN Pregn-4-ene-3,20-dione, 11,17,21-trihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



REFERENCE COUNT: 30
REFERENCE(S):
(1) Ashino-Fuse, H; Int J Cancer 1989, V44, P859 CAPLUS
(2) Barnes, P; Trends Pharmacol Sci 1993, V14, P436 CAPLUS
(5) Blei, F; J Cell Physiol 1993, V155, P568 CAPLUS
(7) Cariou, R; Cell Biol Internat Rep 1988, V12, P1037 CAPLUS
(8) Clark, A; Exp Opin Invest Drugs 1997, V6, P1867 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L110 ANSWER 17 OF 59 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:766507 CAPLUS
DOCUMENT NUMBER: 130:29221
TITLE: Preparation of solid porous matrixes for pharmaceutical uses
INVENTOR(S): Unger, Evan C.
PATENT ASSIGNEE(S): Imarx Pharmaceutical Corp., USA
SOURCE: PCT Int. Appl., 139 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9851282	A1	19981119	WO 1998-US9570	19980512

W: AU, BR, CA, CN, JP, KR, NZ

RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

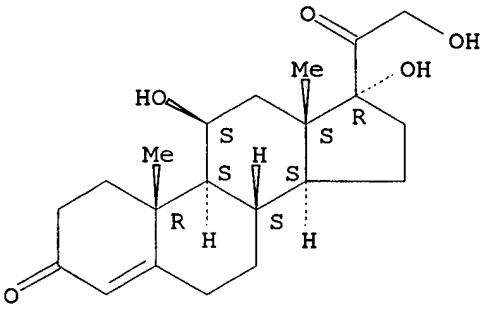
AU 9873787	A1	19981208	AU 1998-73787	19980512
EP 983060	A1	20000308	EP 1998-921109	19980512
R: DE, FR, GB, IT, NL				
PRIORITY APPLN. INFO.:			US 1997-46379	19970513
			US 1998-75477	19980511
			WO 1998-US9570	19980512

AB A solid porous matrix formed from a surfactant, a solvent, and a bioactive agent is described. Thus, amphotericin nanoparticles were prepd. by using ZrO2 beads and a surfactant. The mixt. was milled for 24 h.

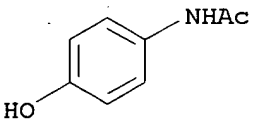
IT **50-23-7 103-90-2, Acetaminophen**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(prepn. of solid porous matrixes for pharmaceutical uses)

RN 50-23-7 CAPLUS
CN Pregn-4-ene-3,20-dione, 11,17,21-trihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 103-90-2 CAPLUS
CN Acetamide, N-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)



REFERENCE COUNT: 1
REFERENCE(S): (1) Wong; US 5569448 A 1996

L110 ANSWER 18 OF 59 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:604841 CAPLUS
DOCUMENT NUMBER: 129:207231
TITLE: Coated implantable medical device
INVENTOR(S): Ragheb, Anthony O.; Bates, Brian L.; Fearnot, Neal E.; Kozma, Thomas G.; Voorhees, William D., III; Gershlick, Anthony H.
PATENT ASSIGNEE(S): Cook Inc., USA
SOURCE: PCT Int. Appl., 44 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

WO 9836784	A1	19980827	WO 1998-US3438	19980220
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9866632	A1	19980909	AU 1998-66632	19980220
EP 968013	A1	20000105	EP 1998-908650	19980220
R: DE, ES, FR, GB, IT				
PRIORITY APPLN. INFO.:			US 1997-38459	19970220
			WO 1998-US3438	19980220

AB A coated implantable medical device includes a structure adapted for introduction into the vascular system, esophagus, trachea, colon, biliary tract, or urinary tract; at least one coating layer posited on one surface of the structure; and at least one layer of a bioactive material posited on at least a portion of the coating layer, wherein the coating layer provides for the controlled release of the bioactive material from the coating layer. In addn., at least one porous layer can be posited over the bioactive material layer, wherein the porous layer includes a polymer and provides for the controlled release of the bioactive material. Preferably, the structure is a coronary stent. The porous layer includes a polymer applied preferably by vapor or plasma deposition and provides a controlled release of the bioactive material. It is particularly preferred that the polymer is a polyamide, parylene or a parylene deriv., which is deposited without solvents, heat or catalysts, and merely by condensation of a monomer vapor. Schematic drawings of the medical device are depicted (no data).

L110 ANSWER 19 OF 59 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:527193 CAPLUS
DOCUMENT NUMBER: 129:166193
TITLE: Therapeutic treatment and prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix
INVENTOR(S): Setterstrom, Jean A.; Van Hamont, John E.; Reid, Robert H.; Jacob, Elliot; Jeyanthi, Ramasubbu; Boedeker, Edgar C.; McQueen, Charles E.; Tice, Thomas R.; Roberts, F. Donald; Friden, Phil
PATENT ASSIGNEE(S): United States Dept. of the Army, USA; Van Hamont, John E.; et al.
SOURCE: PCT Int. Appl., 363 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9832427	A1	19980730	WO 1998-US1556	19980127
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				

Searched by Barb O'Bryen, STIC 308-4291

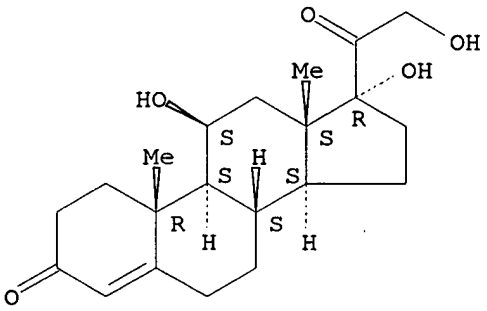
AU 9863175 A1 19980818 AU 1998-63175 19980127
PRIORITY APPLN. INFO.: US 1997-789734 19970127
WO 1998-US1556 19980127

AB Novel burst-free, sustained release biocompatible and biodegradable microcapsules are disclosed which can be programmed to release their active core for variable durations ranging from 1-100 days in an aq. physiol. environment. The microcapsules are comprised of a core of polypeptide or other biol. active agent encapsulated in a matrix of poly(lactide/glycolide) copolymer, which may contain a pharmaceutically acceptable adjuvant, as a blend of upcapped free carboxyl end group and end-capped forms ranging in ratios from 100/0 to 1/99.

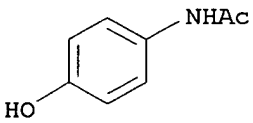
IT **50-23-7, Hydrocortisone 103-90-2, Acetaminophen**
RL: BPR (Biological process); DEV (Device component use); PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(prevention of infections with a bioactive material encapsulated within a biodegradable-biocompatible polymeric matrix)

RN 50-23-7 CAPLUS
CN Pregn-4-ene-3,20-dione, 11,17,21-trihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 103-90-2 CAPLUS
CN Acetamide, N-(4-hydroxyphenyl)- (9CI) (CA INDEX NAME)



L110 ANSWER 20 OF 59 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:430021 CAPLUS
DOCUMENT NUMBER: 129:100034
TITLE: Implantable controlled release device to deliver drugs directly to an internal portion of the body
INVENTOR(S): Ashton, Paul; Pearson, Paul A.
PATENT ASSIGNEE(S): University of Kentucky Research Foundation, USA
SOURCE: U.S., 25 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

Searched by Barb O'Bryen, STIC 308-4291

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 5773019	A	19980630	US 1995-534854	19950927
JP 11512711	T2	19991102	JP 1996-513602	19960926
US 6001386	A	19991214	US 1998-59448	19980414
PRIORITY APPLN. INFO.:			US 1995-534854	19950927
			WO 1996-US15378	19960926

AB A simple and implantable sustained-release drug delivery device has an inner core contg. an effective amt. of a low-soly. active agent covered by a nonbioerodible polymer coating layer that is permeable to the low-soly. active agent. A mammal is treated to obtain a desired local or systemic physiol. or pharmacol. effect by surgically implanting such a sustained-release delivery device. The polymer coating layer holds the drug in the correct anatomical position and prevents disintegration of the drug core while not significantly impairing the drug release rate. The device is suitable for implantation into the eye for treatment of uveitis. Thus, cores contg. 5 mg cyclosporine were coated with several layers of polyvinyl alc., heat treated at 104.degree. for 1 h, inserted into the vitreous body of rabbits, and secured to the sclera. The devices produced steady and sustained ocular levels of cyclosporine (av. 0.50 .mu.g/mL) without significant toxic effects.

L110 ANSWER 21 OF 59 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1998:259042 CAPLUS
DOCUMENT NUMBER: 129:12456
TITLE: Inhibitory effects of tetrandrine on **angiogenesis** in adjuvant-induced chronic inflammation and tube formation of vascular endothelial cells
AUTHOR(S): Kobayashi, Shinjiro; Inaba, Kazuhiko; Kimura, Ikuko; Kimura, Masayasu
CORPORATE SOURCE: Department of Chemical Pharmacology, Faculty of Pharmaceutical Sciences, Toyama Medical and Pharmaceutical University, Toyama, 930-01, Japan
SOURCE: Biol. Pharm. Bull. (1998), 21(4), 346-349
CODEN: BPBLEO; ISSN: 0918-6158
PUBLISHER: Pharmaceutical Society of Japan
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The inhibitory effects of tetrandrine, an alkaloid isolated from the Chinese medicine Stephania tetrandrae S. Moore, were investigated in terms of the **angiogenesis** in an adjuvant-induced chronic inflammation model of mouse and tube formation of rat vascular endothelial cells (EC). Tetrandrine (7.5-30 mg/kg) reduced the carmine content, granuloma wt., inflammatory cell count and pouch fluid wt. in the inflammation model in a dose-dependent manner. The inhibitory pattern of tetrandrine on these parameters was similar to that of **hydrocortisone**. The inhibitory effect of tetrandrine on carmine content was 0.56-fold smaller than that of **hydrocortisone**. Tetrandrine (0.1-10 .mu.M) also inhibited 2% fetal bovine serum (FBS)-stimulated tube formation of vascular EC. The inhibitory effect of tetrandrine on tube formation was more than 100-fold greater than that of **hydrocortisone**. Tetrandrine (10-30 nM) inhibited the tube formation stimulated by interleukin (IL)-1.alpha. and platelet-derived growth factor (PDGF)-BB to a greater extent than FBS-stimulated tube formation. The inhibitory effects of tetrandrine on the action of IL-1.alpha. and PDGF-BB were non-competitive. These results demonstrate that tetrandrine may reduce the tube formation of EC in the **angiogenic** process through inhibition on the post-receptor pathway of IL-1.alpha. and PDGF-BB in chronic inflammation.

L110 ANSWER 22 OF 59 CAPLUS COPYRIGHT 2000 ACS
Searched by Barb O'Bryen, STIC 308-4291

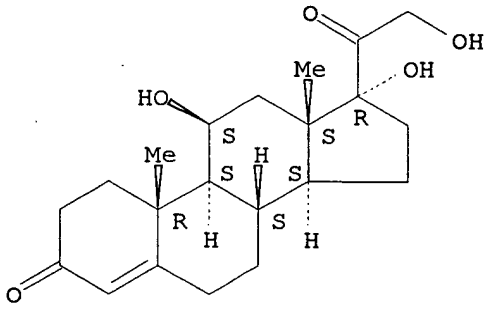
ACCESSION NUMBER: 1998:177000 CAPLUS
DOCUMENT NUMBER: 128:279080
TITLE: Corticosteroids inhibit the expression of the vascular endothelial growth factor gene in human vascular smooth muscle cells
AUTHOR(S): Nauck, Markus; Karakiulakis, George; Perruchoud, Andre P.; Papakonstantinou, Eleni; Roth, Michael
CORPORATE SOURCE: Dep. Clinical Chem., Univ. Hospital, Freiburg, 72085, Germany
SOURCE: Eur. J. Pharmacol. (1998), 341(2/3), 309-315
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The vascular endothelial growth factor (VEGF) is a specific mitogen for vascular endothelial cells and enhances vascular permeability and edemagenesis. VEGF is also a major regulator of **angiogenesis** and may be a key target for inhibiting **angiogenesis** in **angiogenesis**-assocd. diseases. Among the extensively studied **angiostatic** compds. are several corticosteroids when used alone or in combination with heparin. In this study the authors presented evidence for an addnl. mechanism of action of **hydrocortisone**, cortisone and dexamethasone in inhibiting edemagenesis or **angiogenesis**. In cultures of aortic human vascular smooth muscle cells these corticosteroids (1 .times. 10-8 to 1 .times. 10-12 M) abolished the platelet-derived growth factor-induced (PDGF) expression of the VEGF gene in a dose-dependent manner. In contrast, two precursors of corticosteroids, desoxycorticosterone or pregnenolone, did not affect PDGF-induced VEGF expression. The authors' findings indicate that the capacity of corticosteroids to reduce edema or to prevent new blood vessel formation may be attributed, at least in part to the ability of these agents to abolish the expression of VEGF.

IT **50-23-7, Hydrocortisone**
RL: BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(corticosteroids inhibition of VEGF gene expression in human vascular smooth muscle cells in relation to **angiogenesis** and edema inhibition)

RN 50-23-7 CAPLUS
CN Pregn-4-ene-3,20-dione, 11,17,21-trihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L110 ANSWER 23 OF 59 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1997:593792 CAPLUS
DOCUMENT NUMBER: 127:242709
TITLE: **Thalidomide** may impede cell migration in
Searched by Barb O'Bryen, STIC 308-4291

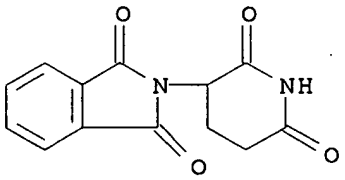
primates by down-regulating integrin .beta.-chains: potential therapeutic utility in solid malignancies, proliferative retinopathy, inflammatory disorders, neointimal hyperplasia, and osteoporosis

AUTHOR(S): Mccarty, M. F.
CORPORATE SOURCE: Nutrition 21, San Diego, CA, 92109, USA
SOURCE: Med. Hypotheses (1997), 49(2), 123-131
CODEN: MEHYDY; ISSN: 0306-9877
PUBLISHER: Churchill Livingstone
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 108 refs. A growing no. of human inflammatory disorders are reported to respond to treatment with **thalidomide**, and recently this drug has been shown to inhibit **angiogenesis** in the rabbit, in doses which can elicit teratogenicity in this species. Studies in marmosets and humans indicate that **thalidomide**, and a teratogenic analog, decrease the expression of .beta. integrin subunits, most notably .beta.3 and the .beta.2 produced by leukocytes. Since integrins are crucial for cell-matrix interactions, and the .beta.2 integrins of leukocytes mediate adhesion to endothelium, it is reasonable to postulate that **thalidomide** inhibits cell migration in susceptible species, and that this accounts for its anti-inflammatory, anti-**angiogenic**, and teratogenic activity. This perspective suggests that **thalidomide** will show utility in the prevention or treatment of a wide range of disorders, including solid tumors, proliferative retinopathies, many inflammatory diseases, neointimal hyperplasia, and osteoporosis. It is likely that dietary fish oil - as well as selective inhibitors of urokinase, when and if they become clin. available - will complement the efficacy of **thalidomide** in most if not all of these applications.

IT **50-35-1, Thalidomide**
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**thalidomide** effect on cell migration: down-regulation of .beta.-integrins and potential therapeutic use in solid malignancies, proliferative retinopathy, inflammatory disorders, neointimal hyperplasia, and osteoporosis)

RN 50-35-1 CAPLUS
CN 1H-Isoindole-1,3(2H)-dione, 2-(2,6-dioxo-3-piperidinyl)- (9CI) (CA INDEX NAME)



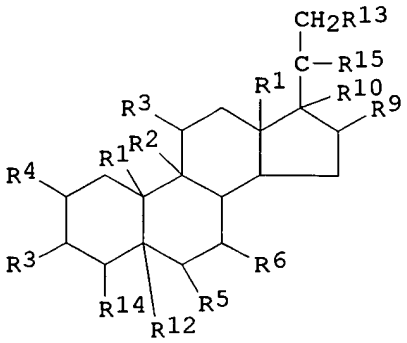
L110 ANSWER 24 OF 59 CAPLUS COPYRIGHT 2000 ACS
ACCESSION NUMBER: 1991:687178 CAPLUS
DOCUMENT NUMBER: 115:287178
TITLE: Ophthalmic composition of **angiostatic** steroid-glucocorticoid combination for treatment of inflammation
INVENTOR(S): Clark, Abbot F.
PATENT ASSIGNEE(S): Alcon Laboratories, Inc., USA
SOURCE: PCT Int. Appl., 16 pp.
Searched by Barb O'Bryen, STIC 308-4291

CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 7
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9103245	A1	19910321	WO 1990-US4071	19900725
W: AU, CA, JP				
RW: AT, BE, CH, DE, DK, ES, FR, GB, IT, LU, NL, SE				
US 4945089	A	19900731	US 1989-399351	19890828
AU 9062952	A1	19910408	AU 1990-62952	19900725
AU 637824	B2	19930610		
EP 489779	A1	19920617	EP 1990-912700	19900725
EP 489779	B1	19980128		
R: AT, BE, CH, DE, DK, FR, GB, IT, LI, LU, NL, SE				
JP 05500054	T2	19930114	JP 1990-512212	19900725
WO 9903503	A1	19990128	WO 1998-US12711	19980618
W: AU, BR, CA, JP, MX, US				
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE				
AU 9881515	A1	19990210	AU 1998-81515	19980618
EP 1003553	A1	20000531	EP 1998-931367	19980618
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI				
BR 9811012	A	20001017	BR 1998-11012	19980618

PRIORITY APPLN. INFO.:
US 1989-399351 19890828
US 1989-419226 19891010
US 1987-139222 19871229
WO 1990-US4071 19900725
US 1997-895184 19970716
WO 1998-US12711 19980618

OTHER SOURCE(S): MARPAT 115:287178
GI



I

AB Pharmaceutical compns. useful in the treatment of ophthalmic inflammation, and methods of treating ophthalmic inflammation with those compns., are disclosed. The compns. contain a combination of a glucocorticoid and an **angiostatic** steroid, e.g. [R1 = .beta.-Me, .beta.-Et; R2 = H, Cl; R3 = H, OH, alkoxy, etc., or R2R3 = O or double bond bridging C-9 and C-11, or R2 = .alpha.-F and R3 = .beta.-OH, or R2 = .alpha.-Cl and R3 = .beta.-Cl; R4 = H, Me, Cl, F; R5 = H, OH, F, Cl, Br, Me, Ph, vinyl, alkyl; R6 = H, Me; R9 = H, OH, Me, F, :CH2; R10 = H, OH, Me, or R10 forms a 2nd

Searched by Barb O'Bryen, STIC 308-4291

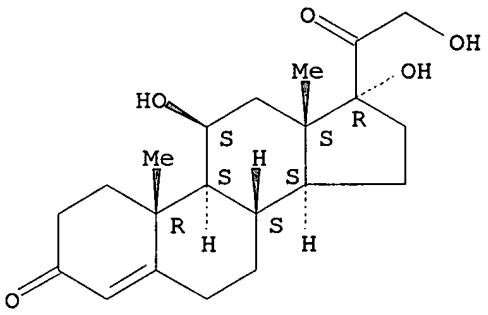
bond between C-16 and C-17; R12 = H or double bond with R14; R13 = H, OH, :O, OP(O)(OH)2, OC(O)(CH2)nCO2H (n = 2-6); R14 = H, double bond with R12; R15 = :O, OH; R23 = OH, OPO(O)(OH)2, etc. (with provisions and exclusions)]. The **angiostatic** steroid substantially prevents any significant increases in intraocular pressure which might otherwise be experienced by the patient as a side effect of the glucocorticoid component of the compns. The therapeutic interaction of the 2 components therefore allows the potent anti-inflammatory properties of the glucocorticoids to be used without fear of elevating intraocular pressure. A formulation contg. tetrahydrocortexolone and dexamethasone is given.

IT **50-23-7D, Hydrocortisone,** mixts. with **angiostatic** steroids
RL: BIOL (Biological study)
(**anti-inflammatory** ophthalmic pharmaceuticals contg.)

RN 50-23-7 CAPLUS

CN Pregn-4-ene-3,20-dione, 11,17,21-trihydroxy-, (11.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L110 ANSWER 25 OF 59 CAPLUS COPYRIGHT 2000 ACS

ACCESSION NUMBER: 1991:505683 CAPLUS

DOCUMENT NUMBER: 115:105683

TITLE: Selective inhibition by magnosalin and magnoshinin, compounds from 'Shin-i' (Flos magnoliae), of adjuvant-induced **angiogenesis** and granuloma formation in the mouse pouch

AUTHOR(S): Kimura, Masayasu; Kobayashi, Shinijiro; Luo, Bao; Kimura, Ikuko

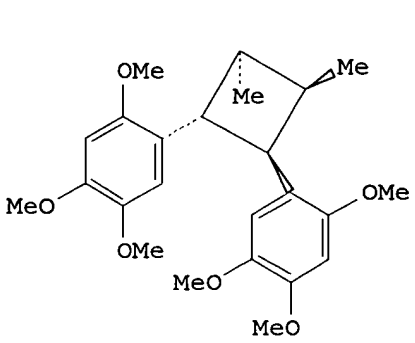
CORPORATE SOURCE: Fac. Pharm. Sci., Toyama Med. Pharm. Univ., Toyama, 930-01, Japan

SOURCE: Int. Arch. Allergy Appl. Immunol. (1990), 93(4), 365-70
CODEN: IAAAAM; ISSN: 0020-5915

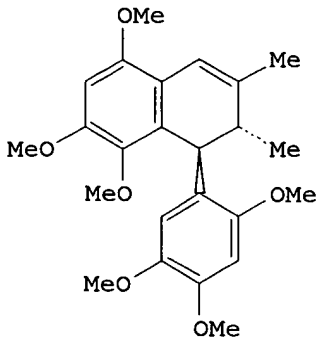
DOCUMENT TYPE: Journal

LANGUAGE: English

GI



I



II

AB Inhibitory effects of magnosalin (I) and magnoshinin (II), compds. from the crude drug 'Shin-i' (Flos magnoliae), on **angiogenesis** and pouch granuloma formation induced by an adjuvant contg. croton oil were investigated. Magnosalin inhibited **angiogenesis** 2.4-fold (intra-pouch) and 9.7-fold (i.p.) more strongly than granuloma formation. The inhibition of **angiogenesis** by magnosalin was 5-fold (intra-pouch) and 21-fold (i.p.) weaker than that by **hydrocortisone**. In contrast, i.p. magnoshinin inhibited granuloma formation 2.5-fold more strongly than **angiogenesis**. The regression coeffs. of anti-**angiogenesis** vs. the inhibition of granuloma formation were 1.79 for magnosalin, 1.11 for **hydrocortisone**, and 0.61 for magnoshinin. Thus, the anti-chronic inflammatory effect of 'Shin-i' was caused by selective inhibition of **angiogenesis** by magnosalin and of granuloma formation by magnoshinin.

L110 ANSWER 26 OF 59 MEDLINE
ACCESSION NUMBER: 2000209416 MEDLINE
DOCUMENT NUMBER: 20209416
TITLE: Curcuminoids inhibit the angiogenic response stimulated by fibroblast growth factor-2, including expression of matrix metalloproteinase gelatinase B.
AUTHOR: Mohan R; Sivak J; Ashton P; Russo L A; Pham B Q; Kasahara N; Raizman M B; Fini M E
CORPORATE SOURCE: Vision Research Laboratories of New England Eye Center and the Department of Ophthalmology, Tufts University School of Medicine, Boston, Massachusetts 02111, USA.
CONTRACT NUMBER: AR42981 (NIAMS)
EY12651 (NEI)
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2000 Apr 7) 275 (14) 10405-12.
Journal code: HIV. ISSN: 0021-9258.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 200007
ENTRY WEEK: 20000702
AB We have studied mechanisms controlling activation of the gelatinase B gene (matrix metalloproteinase-9) by fibroblast growth factor-2 (FGF-2) during angiogenesis, and the effects of the natural product curcuminoids on this process. Using a transgenic mouse (line 3445) harboring a gelatinase B promoter/lacZ fusion gene, we demonstrate FGF-2 stimulation of reporter

gene expression in endothelial cells of invading neocapillaries in the corneal micropocket assay. Using cultured corneal cells, we show that FGF-2 stimulates DNA binding activity of transcription factor AP-1 but not NF-kappaB and that AP-1 stimulation is inhibited by curcuminoids. We further show that induction of gelatinase B transcriptional promoter activity in response to FGF-2 is dependent on AP-1 but not NF-kappaB response elements and that promoter activity is also inhibited by curcuminoids. In rabbit corneas, the angiogenic response induced by implantation of an FGF-2 pellet is inhibited by the co-implantation of a curcuminoid pellet, and this correlates with inhibition of endogenous gelatinase B expression induced by FGF-2. Angiostatic efficacy in the cornea is also observed when curcuminoids are provided to mice in the diet. Our findings provide evidence that curcuminoids target the FGF-2 angiogenic signaling pathway and inhibit expression of gelatinase B in the angiogenic process.

L110 ANSWER 27 OF 59 MEDLINE
ACCESSION NUMBER: 2000199678 MEDLINE
DOCUMENT NUMBER: 20199678
TITLE: Interleukin 12 and indomethacin exert a synergistic, angiogenesis-dependent antitumor activity in mice.
AUTHOR: Golab J; Kozar K; Kaminski R; Czajka A; Marczak M; Switaj T; Giermasz A; Stoklosa T; Lasek W; Zagozdzon R; Mucha K; Jakobisiak M
CORPORATE SOURCE: Department of Immunology, Institute of Biostructure, The Medical University of Warsaw, Poland.. jgolab@ib.amwaw.edu.pl
SOURCE: LIFE SCIENCES, (2000 Feb 18) 66 (13) 1223-30. Journal code: L62. ISSN: 0024-3205.
PUB. COUNTRY: ENGLAND: United Kingdom
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Cancer Journals; Priority Journals
ENTRY MONTH: 200006
AB Nonsteroidal anti-inflammatory drugs have been shown to reduce the incidence and mortality from colorectal cancer. It has recently been demonstrated that these drugs are capable of suppressing the production of pro-angiogenic factors from tumor cells. The mechanisms of antitumor action of interleukin 12 include the enforced secretion of anti-angiogenic factors and stimulation of antitumor immunity. Therefore, we hypothesized that the combination of a model nonsteroidal anti-inflammatory drug--indomethacin and interleukin 12--would result in enhanced angiogenesis-dependent antitumor effects against a colon-26 carcinoma cells transplanted into syngeneic mice. As expected the combined administration of both agents simultaneously resulted in a strengthened antitumor activity that was manifested as a retardation of tumor growth and prolongation of mouse survival. Importantly some mice were completely cured after the combined treatment. As administration of interleukin 12 and indomethacin resulted in enhanced inhibition of angiogenesis it seems possible that prevention of new blood vessel formation is one of the mechanisms responsible for the observed antitumor effects.

L110 ANSWER 28 OF 59 MEDLINE
ACCESSION NUMBER: 2000011629 MEDLINE
DOCUMENT NUMBER: 20011629
TITLE: Topical amiloride accelerates healing and delays neovascularization in mechanically produced corneal ulcers in rabbits.
AUTHOR: Sood A K; Gupta B; Chugh P
CORPORATE SOURCE: Department of Ophthalmology, LLRM Medical College, Meerut, India.
SOURCE: METHODS AND FINDINGS IN EXPERIMENTAL AND CLINICAL

PHARMACOLOGY, (1999 Sep) 21 (7) 491-7.
Journal code: LZN. ISSN: 0379-0355.
PUB. COUNTRY: Spain
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200002
ENTRY WEEK: 20000204
AB The present investigation was undertaken to explore the ulcer healing and antiangiogenic efficacy of two dosage schedules of topically administered amiloride in mechanically produced corneal ulcers in rabbits and to compare its effect with the conventional topical antiinflammatory angiostatic agent flurbiprofen. The epithelium and superficial lamellae of the stroma of both eyes of each rabbit were cut through by a corneal trephine (8 mm diameter) up to a depth of 0.3 mm and removed after local anesthesia. The animals were randomly divided in groups of 4 rabbits each. In the eyes of 2 groups of animals, amiloride (4%) was instilled either q.i.d. or b.i.d.; in another, flurbiprofen (0.03%) was instilled twice daily whereas the saline-treated group served as control. The healing of ulcer was followed on a slit lamp regarding its size, depth, slough formation, infiltration and neovascularization on alternate days up to the 10th day with and without fluorescein staining. Healing of corneal ulcers was significantly accelerated by both dosage schedules of topical amiloride (4%) but more so following q.i.d. instillation. Topical flurbiprofen, on the other hand, delayed the healing process. Instillation of amiloride four times daily or flurbiprofen twice daily inhibited angiogenesis significantly. However, appearance of new vessels was completely prevented when amiloride (4%) was instilled twice daily. Thus topical amiloride (4%) may prove to be a cheap and better antineovascularization as well as ulcer healing agent with no apparent side effects. Inhibition of uPA by amiloride appears to be responsible for these effects.

L110 ANSWER 29 OF 59 MEDLINE
ACCESSION NUMBER: 97032708 MEDLINE
DOCUMENT NUMBER: 97032708
TITLE: Evaluation of angiogenic inhibitors with an in vivo quantitative angiogenesis method using agarose microencapsulation and mouse hemoglobin enzyme-linked immunosorbent assay.
AUTHOR: Okada N; Fushimi M; Nagata Y; Fukunaga T; Tsutsumi Y; Nakagawa S; Mayumi T
CORPORATE SOURCE: Faculty and Graduate School of Pharmaceutical Sciences, Osaka University, Suita.
SOURCE: JAPANESE JOURNAL OF CANCER RESEARCH, (1996 Sep) 87 (9) 952-7.
Journal code: HBA. ISSN: 0910-5050.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199702
ENTRY WEEK: 19970204
AB In the present work, using a previously reported in vivo quantitative tumor-angiogenesis model, we attempted to ascertain whether this animal model is suitable for practical use in monitoring inhibitors of tumor angiogenesis. Mouse sarcoma-180 cells, human A431 cells or rat C6 cells microencapsulated in agarose beads were implanted s.c. into C57BL/6 mice. The level of blood vessel induction at the agarose pellet site was evaluated using mouse hemoglobin enzyme-linked immunosorbent assay on day 10 after implantation. Hydrocortisone, tetrahydro-S, medroxyprogesterone acetate, pentosan polysulfate and suramin inhibited blood vessel growth in

our in vivo tumor-angiogenesis assay system, and heparin enhanced the antiangiogenic effects of hydrocortisone and tetrahydro-S. These results are almost entirely consistent with those observed in common assay systems, and suggest that this method may be useful for the identification and quantitative evaluation of inhibitors of tumor angiogenesis.

L110 ANSWER 30 OF 59 MEDLINE
ACCESSION NUMBER: 96009710 MEDLINE
DOCUMENT NUMBER: 96009710
TITLE: The pharmacological modulation of angiogenesis in chronic granulomatous inflammation.
AUTHOR: Colville-Nash P R; Alam C A; Appleton I; Brown J R; Seed M P; Willoughby D A
CORPORATE SOURCE: Department of Experimental Pathology, Saint Bartholomew's Hospital Medical College, London, United Kingdom..
SOURCE: JOURNAL OF PHARMACOLOGY AND EXPERIMENTAL THERAPEUTICS, (1995 Sep) 274 (3) 1463-72.
Journal code: JP3. ISSN: 0022-3565.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199601
AB Angiogenesis is required for the progression of chronic inflammation, and agents that alter it can affect the development of inflammation and the consequent tissue destruction. However, in vivo quantification of neovascularization and its modulation by angiostatic and angiogenic agents is difficult. Studies have relied on reported effects of drugs on embryonic and tumor vasculature to infer angiomodulatory actions. We have characterized a vascular casting method that incorporates carmine in gelatin. Vascularity expressed as micrograms dye/mg dry tissue (vascularity index, V.I.) was studied in the murine chronic granulomatous air pouch. Carmine was retained within the vasculature by gelatin, and its content increased before the granulomatous tissue, resulting in a V.I. peak at 5 days, regression and a second peak over 14 to 28 days. The modulation of prostaglandin synthesis, plasma exudation and vasomotor tone showed that the carmine V.I. remained unaffected, unlike Evans blue, illustrating independence from acute inflammatory processes such as vasomotor tone and plasma exudation. The angiogenic stimulus p.o. heparin increased the V.I., whereas a sub-anti-inflammatory dose of cortisone with 1000 U heparin reduced it. Higher doses of heparin overcame this. The potent angiostatic steroid tetrahydrocortisol significantly reduced the V.I. in the absence of heparin. Cortisone exhibited independence from heparin on topical administration in hyaluronan. Dexamethasone inhibited granulomatous tissue development with a resulting increase in V.I. These observations indicated the differential effects of angiostatic and anti-inflammatory steroid activity. The pharmacological modulation of angiogenesis in inflammation can therefore be quantified.

L110 ANSWER 31 OF 59 MEDLINE
ACCESSION NUMBER: 94127835 MEDLINE
DOCUMENT NUMBER: 94127835
TITLE: Pentosan inhibits angiogenesis in vitro and suppresses prostate tumor growth in vivo.
AUTHOR: Nguyen N M; Lehr J E; Pienta K J
CORPORATE SOURCE: Meyer L. Prentis Comprehensive Cancer Center, Wayne State University School of Medicine, Michigan Cancer Foundation, Detroit 48201.
CONTRACT NUMBER: CA-57453 (NCI)
CA-60156 (NCI)
SOURCE: ANTICANCER RESEARCH, (1993 Nov-Dec) 13 (6A) 2143-7.
Journal code: 59L. ISSN: 0250-7005.

PUB. COUNTRY: Greece
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals; Cancer Journals
ENTRY MONTH: 199405

AB Pentosan polysulfate (PPS) is a highly negatively charged polysaccharide which has activity against multiple tumor types in the preclinical setting. We demonstrate here that Pentosan inhibits the growth of the anaplastic Dunning R3327 rat prostate adenocarcinoma MAT-LyLu when treatment was started when the tumor was not palpable but has little effect against established tumors. This inhibition may be mediated by the effect of Pentosan on endothelial cells. Pentosan, in combination with hydrocortisone, inhibits endothelial cell motility and tubule formation in vitro and inhibits capillary formation in the chicken chorioallantoic membrane (CAM) assay. These data suggest that Pentosan may be a potent inhibitor of tumor-associated angiogenesis and may be an effective agent for the prevention and/or suppression of prostate cancer growth.

L110 ANSWER 32 OF 59 MEDLINE
ACCESSION NUMBER: 88180604 MEDLINE
DOCUMENT NUMBER: 88180604
TITLE: The prostaglandin and the occurrence of corneal edema and neovascularization in anterior segmental ischemia induced in rabbit eyes.
AUTHOR: Yamane A; Tokura T; Sano T; Miki H
SOURCE: NIPPON GANKA GAKKAI ZASSHI. ACTA SOCIETATIS OPHTHALMOLOGICAE JAPONICAE, (1987 Nov) 91 (11) 1079-85.
Journal code: 220. ISSN: 0029-0203.
PUB. COUNTRY: Japan
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Japanese
ENTRY MONTH: 198807

L110 ANSWER 33 OF 59 MEDLINE
ACCESSION NUMBER: 85148705 MEDLINE
DOCUMENT NUMBER: 85148705
TITLE: The histopathology of corneal neovascularization. Inhibitor effects.
AUTHOR: Robin J B; Regis-Pacheco L F; Kash R L; Schanzlin D J
CONTRACT NUMBER: EY03040 (NEI)
SOURCE: ARCHIVES OF OPHTHALMOLOGY, (1985 Feb) 103 (2) 284-7.
Journal code: 830. ISSN: 0003-9950.
PUB. COUNTRY: United States
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198506

AB With the use of a previously described model of corneal neovascularization induced by thermal cautery, we examined the effects of inhibitors on both the incidence of corneal neovascularization and the degree of inflammatory cell response. Three known inhibitors of corneal neovascularization, 1% prednisolone acetate, indomethacin, and 0.3% flurbiprofen, were studied and the results were compared with those in saline-treated controls. As expected, corneal neovascularization, preceded by conjunctival and corneal polymorphonuclear leukocyte (PMNL) infiltration, occurred in all control animals. Corneal neovascularization did not occur in any of the inhibitor-treated eyes. Histopathologically, both conjunctival and corneal PMNL counts in the treated eyes were markedly reduced compared with controls. These findings are consistent with the hypothesis that inflammatory cells, particularly PMNLs, are closely associated with the initiation of corneal neovascularization.

L110 ANSWER 34 OF 59 MEDLINE
ACCESSION NUMBER: 84081651 MEDLINE
DOCUMENT NUMBER: 84081651
TITLE: Indomethacin v. dexamethasone in the suppression of corneal neovascularization.
AUTHOR: Harvey P T; Cherry P M
SOURCE: CANADIAN JOURNAL OF OPHTHALMOLOGY, (1983 Oct) 18 (6) 293-5. Journal code: CJJ. ISSN: 0008-4182.
PUB. COUNTRY: Canada
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198404
AB A 7-0 silk suture was placed in one of the corneas of each of 18 albino rabbits as a vasogenic stimulus. Two drops of normal saline, a 10.3 mg/ml suspension of indomethacin or a 0.1% suspension of dexamethasone, allocated in double-masked fashion, were then instilled in the 18 eyes three times per day. There was a statistically significant difference (p less than 0.01) in the rate of neovascularization between the 6 control corneas and the 12 treated corneas but no significant difference in the rate or the quality of neovascularization between the 6 indomethacin-treated corneas and the 6 dexamethasone-treated corneas.

L110 ANSWER 35 OF 59 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000220888 EMBASE
TITLE: Infliximab: A review of its use in the management of rheumatoid arthritis.
AUTHOR: Markham A.; Lamb H.M.
CORPORATE SOURCE: H.M. Lamb, Adis International Limited, 41 Centorian Drive, Mairangi Bay, Auckland 10, New Zealand. demail@adis.co.nz
SOURCE: Drugs, (2000) 59/6 (1341-1359).
Refs: 54
ISSN: 0012-6667 CODEN: DRUGAY
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 038 Adverse Reactions Titles
031 Arthritis and Rheumatism
005 General Pathology and Pathological Anatomy
037 Drug Literature Index
030 Pharmacology
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Infliximab is a chimaeric monoclonal antibody to human tumour necrosis factor-.alpha. (TNF.alpha.). It binds to both soluble and transmembrane forms of TNF.alpha. at picomolar concentrations in vitro. Secondary to inhibition of TNF alpha., infliximab reduces serum levels of inflammatory mediators and vascular endothelial growth factor, decreases the expression of chemokines in the synovial tissue and reduces lymphocyte migration into the joints of patients with rheumatoid arthritis. In 2 multicentre randomised double-blind trials conducted over 26 and 30 weeks, infliximab plus methotrexate was significantly more effective than placebo plus methotrexate according to American College of Rheumatology response criteria in patients with active rheumatoid arthritis. A substantial response to infliximab-containing regimens was evident within 2 weeks. Extension phases of these studies indicate sustained clinical efficacy for up to 54 weeks. Of considerable importance are preliminary 1-year radiographic findings that show zero median progression of joint damage in infliximab plus methotrexate recipients compared with a 7 to 8% deterioration in placebo plus methotrexate recipients. Headache, nausea, upper respiratory tract infection and infusion-related reactions are the most commonly reported adverse events with infliximab. Serious events occurred in 4.4% of infliximab versus 1.8% of placebo recipients. In the

largest clinical trial, 2 patients died from disseminated infection and 3 developed new or recurrent malignancies, although the exact relationship between infliximab and these events is unknown. To date, 2 patients with rheumatoid arthritis have developed drug-induced lupus. About 10% of patients may develop antibodies to infliximab, although the clinical significance of these is presently unknown. Conclusion: Infliximab represents an important advance in the treatment of rheumatoid arthritis, with tolerability concerns raised by early studies having been eased somewhat by more recent data in larger patient numbers. If preliminary results indicating that infliximab is able to arrest joint destruction in patients with rheumatoid arthritis are corroborated, the drug will likely become an integral component of future management strategies for this difficult-to-treat condition.

L110 ANSWER 36 OF 59 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000323315 EMBASE
TITLE: Angiogenesis in malignant primary and metastatic brain tumors.
AUTHOR: Reijneveld J.C.; Voest E.E.; Taphoorn M.J.B.
CORPORATE SOURCE: J.C. Reijneveld, Department of Neurology, University Medical Center, P.O. Box 85500, 3508 GA Utrecht, Netherlands. JReijnev@neuro.azu.nl
SOURCE: Journal of Neurology, (2000) 247/8 (597-608).
Refs: 155
ISSN: 0340-5354 CODEN: JNRYA
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
008 Neurology and Neurosurgery
016 Cancer
021 Developmental Biology and Teratology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Patients with malignant primary and metastatic brain tumors have a poor prognosis, despite developments in diagnostic and therapeutic modalities. Therefore in the past decade a search for new therapeutic possibilities has started. The inhibition of angiogenesis, the sprouting of new capillaries from preexisting vasculature, which is an absolute requirement for the growth of tumors beyond a size of a few cubic millimeters, is one of the most promising approaches with which to influence tumor growth. This review focuses on the critical role of angiogenesis in the development of normal brain and the blood-brain barrier. We discuss the importance of angiogenesis in the formation of malignant brain tumors and in blood-brain barrier function in these tumors and possible consequences of altered blood-brain barrier properties for antiangiogenic therapy. Furthermore, results of current clinical trials with antiangiogenic drugs are reviewed, and clinical perspectives of antiangiogenic therapy in malignant brain tumors are outlined.

L110 ANSWER 37 OF 59 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000224680 EMBASE
TITLE: Current status of antiangiogenic factors.
AUTHOR: Talks K.L.; Harris A.L.
CORPORATE SOURCE: Prof. A.L. Harris, Growth Factors Group, Institute of Molecular Medicine, John Radcliffe Hospital, Oxford OX3 9DU, United Kingdom. aharris.lab@icrf.icnet.uk
SOURCE: British Journal of Haematology, (2000) 109/3 (477-489).
Refs: 52
ISSN: 0007-1048 CODEN: BJHEAL
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 025 Hematology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L110 ANSWER 38 OF 59 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000217121 EMBASE
TITLE: Angiogenesis and surgery: From mice to man.
AUTHOR: Drixler T.A.; Voest E.E.; Van Vroonhoven T.J.M.V.; Borel Rinkes I.H.M.
CORPORATE SOURCE: Dr. I.H.M. Borel Rinkes, Department of Surgery, University Medical Center, P.O. Box 85500, NL-3508 GA Utrecht, Netherlands
SOURCE: European Journal of Surgery, (2000) 166/6 (435-446).
Refs: 116
ISSN: 1102-4151 CODEN: EUJSEH
COUNTRY: Norway
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
009 Surgery
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

L110 ANSWER 39 OF 59 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000095414 EMBASE
TITLE: The clinical manipulation of angiogenesis: Pathology, side-effects, surprises, and opportunities with novel human therapies.
AUTHOR: Thompson W.D.; Li W.W.; Maragoudakis M.
CORPORATE SOURCE: W.D. Thompson, Department of Pathology, Univ. of Aberdeen Medical School, Aberdeen Royal Hospitals Trust, Aberdeen AB25 2ZD, United Kingdom. w.d.thompson@abdn.ac.uk
SOURCE: Journal of Pathology, (2000) 190/3 (330-337).
Refs: 55
ISSN: 0022-3417 CODEN: JPTLAS
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The first phase of angiogenesis research has provided knowledge of the basic pathobiology of angiogenesis and its manipulation in models, mouse, and man. The first line of therapeutic substances has been devised and is now in clinical trials. New lessons are being learned from clinical observations. Unexpected side-effects are being noted, particularly affecting the nervous system. Other side-effects may be anticipated from a sound knowledge of clinical pathology and recognition of the commonality of angiogenesis to multiple disease mechanisms, but these may be tolerable or avoidable. Angiogenesis researchers await further feedback and ideas from the clinic to stimulate the next phase of basic and applied research. Copyright (C) 2000 John Wiley and Sons, Ltd.

L110 ANSWER 40 OF 59 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 2000337396 EMBASE
TITLE: The role of selective oestrogen receptor modulators in the treatment of endometrial bleeding in women using long-acting progestin contraception.
AUTHOR: Grow D.R.; Reece M.T.

CORPORATE SOURCE: D.R. Grow, Dept. of Obstetrics and Gynecology, Tufts University, School of Medicine, Springfield, MA 01199, United States. daniel.grow@bhs.org
SOURCE: Human Reproduction, (2000) 15/SUPPL. 3 (30-38).
Refs: 40
ISSN: 0268-1161 CODEN: HUREEE
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 010 Obstetrics and Gynecology
037 Drug Literature Index
038 Adverse Reactions Titles
016 Cancer
030 Pharmacology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB This paper explores the concept that endometrial breakthrough bleeding results from the stimulatory effects of oestrogen in the endometrium. Though 'progestin-only' contraceptive regimens have long been associated with user dissatisfaction because of unpredictable vaginal bleeding, it is likely that the substantial contribution of endogenous ovarian oestradiol during such treatments predisposes the bleeding problems. Oestrogen causes endometrial proliferation, hyperplasia and neoplasia if unopposed. Oestrogen allows production of growth factors supporting angiogenesis which results in an abundance of dilated or fragile endothelial surface blood vessels, predisposing this tissue to bleeding when these vessels lose competence.

L110 ANSWER 41 OF 59 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999373272 EMBASE
TITLE: [Anti-angiogenesis: A new approach in cancer therapy?]. ANTIANGIOGENESE: EIN NEUER ANSATZ IN DER TUMORTHERAPIE?.
AUTHOR: Schiefer D.; Gottstein C.; Diehl V.; Engert A.
CORPORATE SOURCE: Dr. A. Engert, Klin. I fur Innere Medizin der Univ., Bettenhaus Ebene 5, Joseph-Stelzmann-Strasse 9, D-50931 Koln, Germany. a.engert@uni-koeln.de
SOURCE: Medizinische Klinik, (15 Oct 1999) 94/10 (570-579).
Refs: 146
ISSN: 0723-5003 CODEN: MEKLA7
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
016 Cancer
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: German
SUMMARY LANGUAGE: English; German

AB Background: The overall mortality due to metastatic cancer has not or only minimally been reduced in spite of intensive research and many innovations in the field of conventional antineoplastic therapy in the past decade. In the last years it has become a fact that tumor growth is angiogenesis-dependent. Therefore, inhibitors of angiogenesis are a new class of antineoplastic substances with novel mechanism of action that might be a powerful complement to conventional cytostatic therapy. Substances and Clinical Trials: Inhibitors of tumor-angiogenesis which have entered clinical trials, with their results published until December 1998 are discussed here. Most results originate from phase-I or phase-II clinical trials. They are discussed and compared in respect to toxicity and response. Also some substances with high therapeutic potential which are still in preclinical testing are discussed. Results: Many of the investigated angiogenesis inhibitors demonstrated anti-tumor effects in phase-I or phase-II clinical trials. The commonest manifestation was stable disease, followed by partial remissions. In a few cases, complete

remissions were observed. The toxicities of these substances differ both in type and degree of side effects. Conclusion: Some antiangiogenic drugs appear to be promising candidates for a clinical use in the therapy of solid tumors. Further conclusions can only be drawn after evaluation of the results of ongoing phase-III clinical trials.

L110 ANSWER 42 OF 59 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999116728 EMBASE
TITLE: The clinical manipulation of angiogenesis: Pathology, side-effects, surprises, and opportunities with novel human therapies.
AUTHOR: Thompson W.D.; Li W.W.; Maragoudakis M.
CORPORATE SOURCE: W.D. Thompson, Department of Pathology, University of Aberdeen Medical Sch., Aberdeen Royal Hospitals Trust, Aberdeen AB25 2ZD, United Kingdom. w.d.thompson@abdn.ac.uk
SOURCE: Journal of Pathology, (1999) 187/5 (503-510).
Refs: 53
ISSN: 0022-3417 CODEN: JPTLAS
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The first phase of angiogenesis research has provided knowledge of the basic pathobiology of angiogenesis and its manipulation in models, mouse, and man. The first line of therapeutic substances has been devised and is now in clinical trials. New lessons are being learned from clinical observations. Unexpected side-effects are being noted, particularly affecting the nervous system. Other side-effects may he anticipated from a sound knowledge of clinical pathology and recognition of the commonality of angiogenesis to multiple disease mechanisms, but these may be tolerable or avoidable. Angiogenesis researchers await further feedback and ideas from the clinic to stimulate the next phase of basic and applied research.

L110 ANSWER 43 OF 59 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999152448 EMBASE
TITLE: [Impact of angionesis in gynecology and obstetrics]. ANGIOGENESE IN GYNAKOLOGIE UND GEBURTSHILFE.
AUTHOR: Obermair A.; Preyer O.; Leodolter S.
CORPORATE SOURCE: Dr. A. Obermair, Abt. fur Gynakologie/Geburtshilfe, Univ. Klin. fur Frauenheilkunde, Wahringer Gurtel 18-20, A-1090 Wien, Austria. andreas.obermair@akh-wien.ac.at
SOURCE: Wiener Klinische Wochenschrift, (9 Apr 1999) 111/7 (262-277).
Refs: 131
ISSN: 0043-5325 CODEN: WKWOAO
COUNTRY: Austria
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 006 Internal Medicine
010 Obstetrics and Gynecology
037 Drug Literature Index
LANGUAGE: German
SUMMARY LANGUAGE: English; German
AB In current scientific discussion, increasing importance is being given to the clinical significance of the new formation of vessels (angiogenesis) in the course of physiological, inflammatory and neoplastic processes. Angiogenesis is best studied in the growth of malignant tumors, since cancer may be regarded as the most important angiogenesis-dependent disease in terms of social and economic aspects. The significance of angiogenesis in gynecological oncology is as follows: 1) Intratumoral

vessel density is an indicator for the emergence and growth of malignant tumours and their precursor lesions, 2) intratumoral vessel density is an independent prognostic factor for solid malignancies and 3) the inhibition of tumor angiogenesis by means of antiangiogenetic substances causes tumor growth to be suppressed. Angiogenesis also plays an important role in the regulation of the female menstrual cycle. Proliferation of the endometrium and the formation of the corpus luteum in the second half of the menstrual cycle are examples of angiogenesis in the physiological field. The function of angiogenetic factors in the emergence of endometriosis and in female and male infertility are currently under study. In obstetrics, the new formation of blood vessels is significant for the implantation of impregnated blastocysts and for the development and growth of the placenta. Preeclempsia (gestational toxicosis), for instance, is a typical pregnancy-related disease whose pathophysiological mechanism is attributed to a disturbed development and function of small placental vessels. The present paper is an overview of current knowledge and current approaches of research concerning angiogenesis in the field of gynecology and obstetrics. The paper is focused on the clinical significance of angiogenesis.

L110 ANSWER 44 OF 59 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999376368 EMBASE
TITLE: Angiogenesis and arthritis.
AUTHOR: Walsh D.A.
CORPORATE SOURCE: D.A. Walsh, Rheumatology Acad. Univ. Nottingham, Clinical Sciences Building, City Hospital, Hucknall Road, Nottingham NG5 1PB, United Kingdom
SOURCE: Rheumatology, (1999) 38/2 (103-112).
Refs: 144
ISSN: 1462-0324 CODEN: RUMAFK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
031 Arthritis and Rheumatism
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Indices of angiogenesis are increased in synovia from patients with arthritis, and vascular proliferation may contribute to the pathogenesis of synovitis, pannus growth, bone and cartilage destruction, and osteophyte formation. Pharmacological inhibition of angiogenesis therefore has potential as a therapeutic strategy in human arthritis. However, vascular growth is also essential for normal development, female reproduction and tissue repair. Selective inhibition of undesirable angiogenesis requires an understanding of the different regulatory mechanisms in pathological and physiological angiogenesis. This review outlines the evidence that the rate of angiogenesis is increased in the inflamed human synovium, and possible approaches to, and consequences of, the modulation of vascular growth.

L110 ANSWER 45 OF 59 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1999278273 EMBASE
TITLE: The rationale and future potential of angiogenesis inhibitors in neoplasia.
AUTHOR: Gasparini G.
CORPORATE SOURCE: Dr. G. Gasparini, Division of Medical Oncology, Azienda Ospedali Riuniti, Via Melacrino, 89100 Reggio Calabria, Italy. oncologiarc@diel.it
SOURCE: Drugs, (1999) 58/1 (17-38).
Refs: 196
ISSN: 0012-6667 CODEN: DRUGAY
Searched by Barb O'Bryen, STIC 308-4291

COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Malignant tumours are angiogenesis-dependent diseases. Several experimental studies suggest that primary tumour growth, invasiveness and metastasis require neovascularisation. Tumour-associated angiogenesis is a complex multistep process under the control of positive and negative soluble factors. A mutual stimulation occurs between tumour and endothelial cells by paracrine mechanisms. Angiogenesis is necessary, but not sufficient, as the single event for tumour growth. There is, however, compelling evidence that acquisition of the angiogenic phenotype is a common pathway for tumour progression, and that active angiogenesis is associated with other molecular mechanisms leading to tumour progression. Experimental research suggests that it is possible to block angiogenesis by specific inhibitory agents, and that modulation of angiogenic activity is associated with tumour regression in animals with different types of neoplasia. The more promising angiosuppressive agents for clinical testing are: naturally occurring inhibitors of angiogenesis (angiostatin, endostatin, platelet factor-4, and others), specific inhibitors of endothelial cell growth (TNP-470, thalidomide, interleukin-12 and others), agents neutralising angiogenic peptides (antibodies to fibroblast growth factor or vascular endothelial growth factor, suramin and analogues, tecogalan and others) or their receptors, agents that interfere with vascular basement membrane and extracellular matrix [metalloprotease (MMP) inhibitors, angiostatic steroids and others], antiadhesion molecules antibodies such as anti-integrin .alpha.(v).beta.3, and miscellaneous drugs that modulate angiogenesis by diverse mechanisms of action. Antiangiogenic therapy is to be distinguished from vascular targeting. Gene therapy aimed to block neovascularisation is also a feasible anticancer strategy in animals bearing experimental tumours. Antiangiogenic therapy represents one of the more promising new approaches to anticancer therapy and it is already in early clinical trials. Because angiosuppressive therapy is aimed at blocking tumour growth indirectly, through modulation of neovascularisation, antiangiogenic agents need to be developed and evaluated as biological response modifiers. Therefore, adequate and well designed clinical trials should be performed for a proper evaluation of antiangiogenic agents, by determination and monitoring of surrogate markers of angiogenic activity.

L110 ANSWER 46 OF 59 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 1998331456 EMBASE
TITLE: Anti-angiogenic therapies in cancer clinical trials.
AUTHOR: Zhang H.-T.; Harris A.L.
CORPORATE SOURCE: A.L. Harris, Molecular Oncology Laboratories, Imperial Cancer Research Fund, Inst. Mol. Med., Univ. of Oxford, Oxford OX3 9DU. aharris.lab@icrf.icnet.uk
SOURCE: Expert Opinion on Investigational Drugs, (1998) 7/10 (1629-1655).
Refs: 144
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

Searched by Barb O'Bryen, STIC 308-4291

AB Strategies involving vasculature have widely been acknowledged to have therapeutic potential in the management of cancer of other diseases. Based on a large body of evidence from preclinical studies and early clinical trials there is considerable optimism that anti-angiogenesis and vascular targeting will be a major clinical therapy. This review considers some 30 anti-angiogenic and vascular targeting agents that are currently in cancer clinical trials and highlights specific problems relating to the assessment of the activity of these agents in patients, trial design, potential toxicities and resistance mechanisms.

L110 ANSWER 47 OF 59 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97293159 EMBASE
DOCUMENT NUMBER: 1997293159
TITLE: [Angiogenesis and inhibition of angiogenesis in the eye]. ANGIOGENESE UND ANGIOGENESEHEMMUNG IM AUGE.
AUTHOR: Cursiefen C.; Schonherr U.
CORPORATE SOURCE: Dr. C. Cursiefen, APFAU, Erlangen-Nurnberg, Kopfklinikum, Schwabachanlage 6, D-91054 Erlangen, Germany
SOURCE: Klinische Monatsblatter fur Augenheilkunde, (1997) 210/6 (341-351).
Refs: 104
ISSN: 0023-2165 CODEN: KMAUAI
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 012 Ophthalmology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: German
SUMMARY LANGUAGE: German; English
AB Background: Angiogenesis is the formation of new blood vessels from preexisting vessels. Anglogenesis plays an important physiologic and pathologic role in the eye. Pathologic anglogenesis can be found in major causes of human blindness as in diabetic retinopathy and age-related-maculopathy. In recent years great progress has been made in recognizing the mechanisms and regulation of anglogenesis. Results: The general mechanism and the regulation of anglogenesis with proliferative diabetic retinopathy as an example of ocular angiogenesis are reviewed according to recent literature. Angiogenic and antiangiogenic factors regulate the neovascularization. Recent research has identified the vascular endothelial growth factor as the most important mediator of ocular angiogenesis. As well in diabetic retinopathy as in age-related-maculopathy the vascular endothelial growth factor plays a role. New knowledge about ocular anglogenesis is linked to the chance of new antiangiogenie therapies in neovascularizing eye diseases. There exist two ways of ocular antiangiogenic therapy: the first way is to block ocular angiogenic factors such as vascular endothelial growth factor, the other way is to influence the interaction between endothelial cells and extracellular matrix of the newly forming vessels. Conclusion: Recent progress in angiogenesis research could result in new causal antiangiogenic drug therapy in ophthalmology. There are some promising animal experiments of local and systemic antiangiogenic therapy. Because of its anatomic localisation the eye is especially suitable for topic anti-angiogenic therapy.

L110 ANSWER 48 OF 59 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 97000517 EMBASE
DOCUMENT NUMBER: 1997000517
TITLE: Angiogenesis inhibition as a drug target for disease: An update.
AUTHOR: Seed M.P.
CORPORATE SOURCE: M.P. Seed, Dept. of Experimental Pathology, William Harvery Research Institute, Royal School of Medicine/Dentistry,

Charterhouse Square, London EC1M 6BQ, United Kingdom
SOURCE: Expert Opinion on Investigational Drugs, (1996) 5/12 (1617-1637).
ISSN: 1354-3784 CODEN: EOIDER
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
013 Dermatology and Venereology
016 Cancer
029 Clinical Biochemistry
031 Arthritis and Rheumatism
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB Angiogenesis is required for the development of many proliferative diseases, including granulomatous disease, such as rheumatoid arthritis, psoriasis and neoplasia, as well as diabetic retinopathy. A substantial effort is being made to develop inhibitors of angiogenesis for the treatment of these diseases. This article is an update of a previous review [Colville-Nash and Seed, Curr. Opin. Invest. Drugs (1993) 2:763-813], and reviews the recent developments in the use of: angiostatic steroids, fumagillol derivatives, somatostatin analogues, matrix metalloproteinase (MMP) inhibitors, modulators of vascular endothelial cell growth factor (VEGF), fibroblast growth factor (FGF), angiostatin, endostatin, platelet factor-4 (PF4), thrombospondin-1 (TSP-1), cell adhesion molecules (integrins and selectins), urokinase plasminogen receptor antagonists, cyclo-oxygenase (COX) and non-steroidal anti-inflammatory drugs (NSAIDs), nitric oxide synthase (NOS), cytokine-suppressing anti-inflammatory drugs (CSAIDs), and drug combinations. Most of these approaches have been shown to be effective in inhibiting tumour growth in vivo, and many in models of inflammation. The field has, therefore, a very wide range of effective drug targets which are being exploited. Many areas are still limited by their reliance on high molecular weight molecular technologies, antibodies and constructs; however, low molecular weight compounds are now being sought in areas such as cytokine suppression, VEGF, MMPs, COX, NOS, and adhesion molecules. Angiostatic therapy is a rapidly advancing, therapeutically viable and exciting field.

L110 ANSWER 49 OF 59 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95178330 EMBASE
DOCUMENT NUMBER: 1995178330
TITLE: Angiogenesis and cancer metastases: Therapeutic approaches.
AUTHOR: Teicher B.A.
CORPORATE SOURCE: Dana-Farber Cancer Institute, 44 Binney Street,Boston, MA 02115, United States
SOURCE: Critical Reviews in Oncology/Hematology, (1995) 20/1-2 (9-39).
ISSN: 1040-8428 CODEN: CCRHEC
COUNTRY: Ireland
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
037 Drug Literature Index
LANGUAGE: English

L110 ANSWER 50 OF 59 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 95067085 EMBASE
DOCUMENT NUMBER: 1995067085
TITLE: Consequences of angiogenesis for tumor progression, metastasis and cancer therapy.
AUTHOR: Rak J.W.; St. Croix B.D.; Kerbel R.S.

CORPORATE SOURCE: Division of Cancer Research, Sunnybrook Health Science Centre, Reichmann Research Building, S-218, 2075 Bayview Avenue,Toronto, Ont. M4N 3M5, Canada
SOURCE: Anti-Cancer Drugs, (1995) 6/1 (3-18).
ISSN: 0959-4973 CODEN: ANTDEV
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
016 Cancer
022 Human Genetics
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB The growth of solid tumors to a clinically relevant size is dependent upon an adequate blood supply. This is achieved by the process of tumor stroma generation where the formation of new capillaries is a central event. Progressive recruitment of blood vessels to the tumor site and reciprocal support of tumor expansion by the resulting neovasculature are thought to result in a self-perpetuating loop helping to drive the growth of solid tumors. The development of new vasculature also allows an 'evacuation route' for metastatically-competent tumor cells, enabling them to depart from the primary site and colonize initially unaffected organs. Several molecular and cellular mechanisms have been identified by which tumor parenchyma may exert its angiogenic effect on host endothelial cells. As a result of this paracrine influence, tumor-associated endothelial cells acquire an 'immature' phenotype manifested by rapid proliferation, migration, release of proteases and expression of cytokines, endothelial-specific tyrosine kinases (e.g. flk-1, tek and others) as well as numerous other molecular alterations. Consequently a network of structurally and functionally aberrant blood vessels is formed within the tumor mass. There is also evidence that endothelial cells themselves, and likewise other stromal cells, may act reciprocally to alter the behavior of adjacent tumor cells in a paracrine or cell contact mediated fashion. For example, production of interleukin 6(IL-6) by endothelial cells may have a differential effect on human melanoma cells expressing different degrees of aggressiveness. In this manner endothelial derived cytokines could conceivably contribute to tumor progression by suppressing the growth of the less aggressive tumor cells and promoting dominance of their malignant counterparts in 'strategic' perivascular zones. Distinct biological features expressed by tumor-associated vasculature may serve as potential prognostic markers of disease progression as well as novel targets for therapeutic intervention.

L110 ANSWER 51 OF 59 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 94338424 EMBASE
DOCUMENT NUMBER: 1994338424
TITLE: Final discussion.
AUTHOR: Willoughby D.; Falk R.E.; Asculai S.S.; Turley E.; Gustafson S.; Martin G.; Russell A.; Fraser R.; Seed M.P.; Wagener H.H.; Moore A.; Tomlinson A.
CORPORATE SOURCE: Department of Experimental Pathology, Med College St Bartholomew's Hosp, Charterhouse Square,London EC1M 6BQ, United Kingdom
SOURCE: Round Table Series - Royal Society of Medicine, (1994) -/33 (76-87).
ISSN: 0268-3091 CODEN: RTSSES
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 008 Neurology and Neurosurgery
030 Pharmacology
Searched by Barb O'Bryen, STIC 308-4291

037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English

L110 ANSWER 52 OF 59 EMBASE COPYRIGHT 2000 ELSEVIER SCI. B.V.
ACCESSION NUMBER: 92039173 EMBASE
DOCUMENT NUMBER: 1992039173
TITLE: Angiogenesis and its inhibition: Potential new therapies in oncology and non-neoplastic diseases.
AUTHOR: Billington D.C.
CORPORATE SOURCE: Institut de Recherches Servier, 11 Rue des Moulineaux, 92150 Suresnes, France
SOURCE: Drug Design and Discovery, (1991) 8/1 (3-35).
ISSN: 1055-9612 CODEN: DDDIEV
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
018 Cardiovascular Diseases and Cardiovascular Surgery
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The ability to mount an angiogenic response is probably present in all tissues, and stimulation of endothelial cells by any one of a wide variety of factors initiates a cascade of events leading to angiogenesis. In most tissues the overall lack of angiogenesis in normal situations probably results from the interaction of a complex series of multifactorial systems, each of which maintained in a state of balance between stimulation and inhibition. An imbalance in any one these systems, for example by an increase in the concentration of a growth factor, may lead to angiogenesis. Inhibition of angiogenic stimuli is unlikely to be effective as an approach to new angiostatic drugs, given the multiple stimulatory pathways available. Tumour cells for example may induce angiogenesis via release of nuemerous growth factors, prostaglandins ect, and by their attraction of inflammatory cells which in turn release multiple angiogenic stimuli. Inhibitory modulation of many of the individual steps of capillary growth which occur following an angiogenic stimulus can block the angiogenic response. This leads to the expectation that an effective inhibitor of a single key step in this cascade would be able to completely suppress angiogenesis. Inappropriate angiogenesis is an important factor in many disease including cancer and arthritis. In particular angiogenesis is an absolute requirement for neoplastic growth of solid tumours, and the establishment of secondary growths. There is also a strong link between induction of angiogenesis by a tumour and its ability to metastasise.

L110 ANSWER 53 OF 59 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1998-040688 [04] WPIDS
DOC. NO. CPI: C1998-013504
TITLE: Polyethylene glycol ester prodrugs of steroidal and non-steroidal agents - used as e.g. anti-inflammatories, anti-viral agents, immunomodulators, anti-tumour agents and to inhibit neovascularisation..
DERWENT CLASS: A96 B02 B04 B05
INVENTOR(S): ASHTON, P; CONKLIN, J D; CROOKS, P A; CYNKOWSKA, G; CYNKOWSKI, T; GLAVINOS, P G; RIGGS, R M; SMITH, T J
PATENT ASSIGNEE(S): (KENT) UNIV KENTUCKY RES FOUND
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 5681964	A	19971028	(199804)*		22

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 5681964	A	Cont of	US 1990-601644	19901023
		Cont of	US 1993-16179	19930211
		CIP of	US 1993-162388	19931207
			US 1994-318160	19941005

PRIORITY APPLN. INFO: US 1994-318160 19941005; US 1990-601644 19901023; US 1993-16179 19930211; US 1993-162388 19931207

AB US 5681964 A UPAB: 19980126

A polyethylene glycol ester prodrug comprises a steroidal, antiviral, immunomodulating, anti-tumour, neovascular or nonsteroidal compound. The non-steroidal compound is indomethacin, dideoxyinosine (DDI) and gancyclovir and the compound is linked via an ester linkage to a polyethylene glycol of formula HO(CH2CH2)nH where n = 2-12.

USE - The prodrugs are used to treat disease conditions or symptoms e.g. they can be used as anti-inflammatories, antivirals, immunomodulators, anti-tumour agents, to inhibit e.g. neovascularisation.

ADVANTAGE - The prodrug in the case of flurbiprofen is non-irritating unlike flurbiprofen itself.

Dwg.0/0

L110 ANSWER 54 OF 59 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1996-412570 [41] WPIDS
DOC. NO. CPI: C1996-129990
TITLE: Inhibition of mammalian hair growth without side effects - uses e.g. **non-steroidal** suppressor of **angiogenesis**, esp. useful for women with hirsutism.
DERWENT CLASS: B04 B05 D21
INVENTOR(S): AHLUWALIA, G S; SHANDER, D; STYCZYNSKI, P; STYCZNSKI, P
PATENT ASSIGNEE(S): (HAND-I) HANDELMAN J H; (AHLU-I) AHLUWALIA G S; (SHAN-I) SHANDER D; (STYC-I) STYCZYNSKI P
COUNTRY COUNT: 72
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9626712	A2	19960906	(199641)*	EN	24
RW: AT BE CH DE DK EA ES FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG					
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN					
AU 9653009	A	19960918	(199701)		
WO 9626712	A3	19961121	(199702)		
ZA 9601600	A	19961129	(199702)		24
EP 812185	A1	19971217	(199804)	EN	
R: AT BE CH DE DK ES FR GB GR IE IT LI LU NL PT SE					
MX 9706522	A1	19971101	(199902)		
BR 9607060	A	19981215	(199905)		
JP 11501035	W	19990126	(199914)		31
AU 719106	B	20000504	(200030)		
US 6093748	A	20000725	(200038)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9626712	A2		WO 1996-US2790	19960227
AU 9653009	A		AU 1996-53009	19960227
WO 9626712	A3		WO 1996-US2790	19960227
ZA 9601600	A		ZA 1996-1600	19960228
EP 812185	A1		EP 1996-909552	19960227
			WO 1996-US2790	19960227
MX 9706522	A1		MX 1997-6522	19970827
BR 9607060	A		BR 1996-7060	19960227
			WO 1996-US2790	19960227
JP 11501035	W		JP 1996-526415	19960227
			WO 1996-US2790	19960227
AU 719106	B		AU 1996-53009	19960227
US 6093748	A	Cont of	US 1995-396446	19950228
			US 1997-963227	19971103

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9653009	A	Based on	WO 9626712
EP 812185	A1	Based on	WO 9626712
BR 9607060	A	Based on	WO 9626712
JP 11501035	W	Based on	WO 9626712
AU 719106	B	Previous Publ.	AU 9653009
		Based on	WO 9626712

PRIORITY APPLN. INFO: US 1995-396446 19950228; US 1997-963227 19971103

AB WO 9626712 A UPAB: 19961011

Inhibiting mammalian hair growth comprises: (a) selecting an area of skin from which reduced hair growth is desired, and (b) applying to the area a compsn. which comprises a **non-steroidal** suppressor of **angiogenesis**.

USE - The inhibitor can be used to reduce hair growth, esp. in a woman with hirsutism (claimed). The concn. of the suppressor in the compsn. is 1-30 wt.% and should be applied at 100-300 mug/cm2 skin, (claimed).

ADVANTAGE - Use of this compsn. does not cause nicks and cuts, increase hair regrowth, is not expensive, painful, irritate, leave scarring or have unwanted side effects. Use of the compsn. causes a redn. in hair growth of 20 (pref. 70) % when tested in the golden syrian hamster assay.

Dwg.0/1

L110 ANSWER 55 OF 59 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1996-069183 [08] WPIDS
CROSS REFERENCE: 1994-341470 [42]
DOC. NO. CPI: C1996-022569
TITLE: Inhibition, control and regression of **angiogenesis** - using a compsn. comprising a **non-steroidal** antiinflammatory agent and hyaluronic acid.
DERWENT CLASS: B04 B05
INVENTOR(S): ALAM, C; ASCULAI, S S; FALK, R E; HARPER, D W; WILLOUGHBY, D A
PATENT ASSIGNEE(S): (NORP-N) NORPHARMCO INC; (HYAL-N) HYAL PHARM CORP
COUNTRY COUNT: 2
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG

CA 2121454	A	19951016 (199608)*	53
TW 316236	A	19970921 (199805)	

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
CA 2121454	A	CA 1994-2121454	19940415
TW 316236	A	TW 1994-104576	19940520

PRIORITY APPLN. INFO: CA 1994-2121454 19940415; WO 1994-CA207 19940415

AB CA 2121454 A UPAB: 19980202
The use is claimed of a compsn. comprising: (a) a non-steroidal antiinflammatory agent (NSAID), and (b) hyaluronic acid and/or salts, homologues, analogues, derivs., complexes, esters, fragments and/or subunits of hyaluronic acid; for inhibiting, controlling and regressing angiogenesis.

USE - The compsn. can be used to treat subretinal neovascularisation, arthritis, pannus, tumours and as an adjuvant to cancer treatment for prevention of metastasis. For systemic admin. dose of NSAID for a 70kg person is 15-100mg, but may be more (e.g. 420mg, i.e. 60mg/kg) provided that amts. are non-toxic. At least 50 mg hyaluronic acid is used for every 15mg NSAID. Pref. 15-100 mg NSAID is used with sodium hyaluronate in excess of 200 mg, or 400 mg NSAID is used with in excess of 2000 mg hyaluronic acid. For topical application, the amt. of e.g. diclofenac sodium and sodium hyaluronate may each be in excess of 5-10 mg/cm2 of skin or exposed tissue. Treatment is administered daily for a period of weeks.

ADVANTAGE - The compsn. provides greater inhibition, control and regression of angiogenesis than hyaluronic acid alone, and side effects of NSAIDs are reduced by admin. with hyaluronic acid.

Dwg.0/4

L110 ANSWER 56 OF 59 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1994-341470 [42] WPIDS
CROSS REFERENCE: 1996-069183 [08]
DOC. NO. CPI: C1994-155499
TITLE: ~~Compsn. for inhibition, control and~~ regression of ~~angiogenesis~~ - comprises **non steroidal** antiinflammatory ~~agent~~ and hyaluronic ~~acid, useful for treating~~ e.g. sub-retinal neovascularisation, arthritis etc..
DERWENT CLASS: B04 B05
INVENTOR(S): ALAM, C; ASCULAI, S S; FALK, R E; HARPER, D W; WILLOUGHBY, D A; ALLUM, C; WILLOUGHBY, D; WILLOUGHBY, D B
PATENT ASSIGNEE(S): (HYAL-N) HYAL PHARM CORP; (NORP-N) NORPHARMCO INC
COUNTRY COUNT: 58
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9423725	A1	19941027	(199442)*	EN	46
RW: AT BE CH DE DK ES FR GB GR IE IT LU MC NL OA PT SE					
W: AT AU BB BG BR BY CA CH CN CZ DE DK ES FI GB GE HU JP KG KP KR KZ LK LU LV MD MG MN MW NL NO NZ PL PT RO RU SD SE SI SK TJ TT UA US UZ VN					
CA 2094203	A	19941017	(199503)		
AU 9465616	A	19941108	(199507)		
ZA 9402597	A	19950426	(199522)		45
FI 9504914	A	19951106	(199605)		

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NO 9504073 A 19951204 (199606)
TW 264384 A 19951201 (199608)
EP 695187 A1 19960207 (199610) EN
R: AT BE CH DE DK ES FR GB GR IE IT LI LU MC NL PT SE
BR 9405781 A 19960116 (199611)
CZ 9502679 A3 19961016 (199648)
JP 08508505 W 19960910 (199704) 59
HU 74462 T 19961230 (199714)
SK 9501265 A3 19970305 (199729)
CN 1123005 A 19960522 (199746)#
TW 316236 A 19970921 (199805)
SG 48924 A1 19980518 (199834)
AU 694113 B 19980716 (199840)
AU 9869941 A 19980723 (199841)
US 5847002 A 19981208 (199905)
IL 109293 A 19990126 (199911)

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 9423725	A1		WO 1994-CA207	19940415
CA 2094203	A		CA 1993-2094203	19930416
AU 9465616	A		AU 1994-65616	19940415
ZA 9402597	A		ZA 1994-2597	19940415
FI 9504914	A		WO 1994-CA207	19940415
			FI 1995-4914	19951016
NO 9504073	A		WO 1994-CA207	19940415
			NO 1995-4073	19951013
TW 264384	A		TW 1993-106135	19930731
EP 695187	A1		EP 1994-913464	19940415
			WO 1994-CA207	19940415
BR 9405781	A		BR 1994-5781	19940415
			WO 1994-CA207	19940415
CZ 9502679	A3		CZ 1995-2679	19940415
JP 08508505	W		JP 1994-522574	19940415
			WO 1994-CA207	19940415
HU 74462	T		WO 1994-CA207	19940415
			HU 1995-113	19940415
SK 9501265	A3		WO 1994-CA207	19940415
			SK 1995-1265	19940415
CN 1123005	A		CN 1994-192096	19940515
TW 316236	A		TW 1994-104576	19940520
SG 48924	A1		SG 1996-3804	19940415
AU 694113	B		AU 1994-65616	19940415
AU 9869941	A	Div ex	AU 1994-65616	19940415
			AU 1998-69941	19980605
US 5847002	A	Div ex	US 1995-448504	19950605
			US 1995-461123	19950605
IL 109293	A		IL 1994-109293	19940411

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9465616	A	Based on	WO 9423725
EP 695187	A1	Based on	WO 9423725
BR 9405781	A	Based on	WO 9423725
JP 08508505	W	Based on	WO 9423725
HU 74462	T	Based on	WO 9423725
AU 694113	B	Previous Publ.	AU 9465616
		Based on	WO 9423725

PRIORITY APPLN. INFO: CA 1993-2094203 19930416; CN 1994-192096 19940515; CA 1994-2121454 19940415

AB WO 9423725 A UPAB: 19981021

Compsn. for inhibiting, controlling and/or regressing **angiogenesis** comprises therapeutically acceptable amts. of: (a) a non-**steroidal** antiinflammatory agent (**NSAID**); and (b) hyaluronic acid and/or its salts, homologues, analogues, derivs., complexes, esters, fragments, and sub-units of hyaluronic acid.

Pref., the hyaluronic acid is sodium hyaluronate (molecular wt. less than about 750000 daltons). The NSAID is diclofenac, diclofenac sodium, indomethacin, naproxen, (+/-)-tromethamine salt of ketorolac, ibuprofen (RTM), piroxicam (RTM), propionic acid derivs., acetylsalicylic acid or flunixin.

USE - The compsn. is useful for treatment of sub-retinal neovascularisation, arthritis or pannus, or tumours, and as an adjunct to cancer treatment. For a 70 kg patient, the systemic dose of NSAID, e.g. diclofenac, is 15-100 mg, or larger amts. e.g. 420 mg. For every 15 mg NSAID, about 50 mg of the hyaluronic acid is used, i.e. about 50-1050 mg. Partic. pref. is 420 mg diclofenac with 220 mg sodium hyaluronate. For topical admin., the amt. of e.g. both diclofenac sodium and sodium hyaluronate is in excess of 5-10 mg/cm2 of skin or exposed tissue. Treatment is administered daily for a number of weeks.

Dwg.0/4

L110 ANSWER 57 OF 59 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1990-217294 [29] WPIDS
DOC. NO. CPI: C1990-093840
TITLE: Angiostatic pharmaceutical compsn. - contg. dextran sulphate or beta-1,3-glycan sulphate and opt. **steroidal** or **non-steroidal** cpd. to accelerate **angiostatic** activity.
DERWENT CLASS: B05
INVENTOR(S): KANAMARU, T; NOZAKI, Y; SUDO, K
PATENT ASSIGNEE(S): (KANA-I) KANAMARU T; (TAKE) TAKEDA CHEM IND LTD
COUNTRY COUNT: 3
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
CA 2002814	A	19900516	(199029)*		
JP 02223525	A	19900905	(199042)		
US 5135920	A	19920804	(199234)		7

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
CA 2002814	A	CA 1989-2002814	19891114
JP 02223525	A	JP 1989-285799	19891031
US 5135920	A	US 1989-434440	19891109

PRIORITY APPLN. INFO: JP 1988-289782 19881116

AB CA 2002814 A UPAB: 19930928

A pharmaceutical compsn. contains dextransulphate (II) or a B-1,3-glycan sulphate (I) or a salt of one of these cpds. and a carrier diluent or excipient. It may also contain a steroidal or non-steroidal substance to accelerate the argiostatic activity of (I) or (II).

USE - The compsn. is for the treatment or prevention of diseases caused by abnormally accelerated angiogenesis. Daily oral or parenteral dosages of (I) or (II) are generally in the range 10-900 mg.

0/0

L110 ANSWER 58 OF 59 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD
ACCESSION NUMBER: 1989-233735 [32] WPIDS
CROSS REFERENCE: 1993-066455 [08]; 1993-182233 [22]; 1993-377468 [47]; 1995-292509 [38]; 1996-251040 [25]; 1996-464758 [46]; 1997-212558 [19]; 1997-212585 [19]
DOC. NO. CPI: C1989-104075
TITLE: Compsn. inhibiting undesired or pathological cell or tissue growth - contains cyclodextrin deriv. with latent growth-inhibiting steroid or non-steroidal growth inhibitor.
DERWENT CLASS: A96 B01 B03
INVENTOR(S): FOLKMAN, M J; WEISZ, P B
PATENT ASSIGNEE(S): (CHIL-N) CHILDREN'S HOSPITAL CORP; (UYPE-N) UNIV PENNSYLVANIA; (FOLK-I) FOLKMAN M J; (WEIS-I) WEISZ P B
COUNTRY COUNT: 20
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 8906536	A	19890727	(198932)*	EN	43
RW: AT BE CH DE FR GB IT LU NL SE					
W: AU DK GB JP KR					
AU 8930327	A	19890811	(198944)		
CN 1036135	A	19891011	(199031)		
DK 9001713	A	19900821	(199046)		
EP 398925	A	19901128	(199048)		
R: AT BE CH DE FR GB IT LI LU NL SE					
ES 2017808	A	19910301	(199115)		
US 5019562	A	19910528	(199124)		16
IL 88970	A	19930513	(199324)		
EP 398925	B1	19931020	(199342)	EN	12
R: AT BE CH DE FR GB IT LI LU NL SE					
DE 68910113	E	19931125	(199348)		
EP 398925	A4	19910703	(199517)		
IE 64346	B	19950728	(199538)		
JP 2995069	B2	19991227	(200006)		17

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 8906536	A	WO 1989-US175	19890117
EP 398925	A	EP 1989-901794	19890117
ES 2017808	A	ES 1989-157	19890117
US 5019562	A	US 1989-434659	19891109
IL 88970	A	IL 1989-88970	19890117
EP 398925	B1	EP 1989-901794	19890117
		WO 1989-US175	19890117
DE 68910113	E	DE 1989-610113	19890117
		EP 1989-901794	19890117
		WO 1989-US175	19890117
EP 398925	A4	EP 1989-901794	
IE 64346	B	IE 1989-125	19890117
JP 2995069	B2	JP 1989-501676	19890117
		WO 1989-US175	19890117

FILING DETAILS:

PATENT NO	KIND	PATENT NO

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EP 398925	B1	Based on	WO 8906536
DE 68910113	E	Based on	EP 398925
		Based on	WO 8906536
JP 2995069	B2	Previous Publ.	JP 03502323
		Based on	WO 8906536

PRIORITY APPLN. INFO: US 1989-295638 19890110; US 1988-145407 19880119; US 1989-434659 19891109

AB WO 8906536 A UPAB: 20000203

Compsn. for inhibiting undesired or pathological cell or tissue growth, including angiogenesis, in humans and mammals comprises: (i) a deriv. (I) of alpha-beta-or gamma- cyclodextrin; and (i) a latent growth-inhibiting steroid (IIa) or a non-steroidal growth -inhibiting organic cpd. (IIb) in which (I) is characterised by a solubility at 0 deg.C in distilled water of at least 20g/100 ml.

USE/ADVANTAGE - Useful for controlling or eliminating tumours, e.g. reticulum cell sarcona, Lewis lung carciona B-16 melamona, bladder carciona, etc., for treating rheumatoid arthritis, haemangionas, angiofibromes, psoriasis, diabetic retinopathy, retrolental fibroplasia and neovascular glaucoma; and for inhibiting undesired smooth muscle cell development following angioplasty or treatment to remove atherosclerotic plaques. The cyclodextrin replaces heparin inthe combination, avoiding undesired anticoagulant effects and giving a more predictable activity, since heparin activity caries with source and isolation process etc. Unlike heparin, no activation of angiogenesis is observed at higher doses. Antiangiogenic activity may be potentiated.

Dwg.0/5

L110 ANSWER 59 OF 59 WPIDS COPYRIGHT 2000 DERWENT INFORMATION LTD

ACCESSION NUMBER:	1989-214411 [30] WPIDS
CROSS REFERENCE:	1993-066455 [08]; 1996-251040 [25]
DOC. NO. CPI:	C1989-095328
TITLE:	Use of fumagillin as angiogenesis inhibitor - e.g. in treatment of diabetic retinopathy, neovascular glaucoma, ocular tumours, wound granulation, vascular adhesions, etc..
DERWENT CLASS:	A96 B01 B03
INVENTOR(S):	FOLKMAN, M J; WEISZ, P B; FOLKMAN, J; FUJITA, T; INGBER, D; KANAMARU, T
PATENT ASSIGNEE(S):	(CHIL-N) CHILDREN'S HOSPITAL CORP; (UYPE-N) UNIV PENNSYLVANIA; (CHIL-N) CHILDRENS MEDICAL CENT; (TAKE) TAKEDA CHEM IND LTD; (CHIL-N) CHILDREN'S MED CENT CORP; (FOLK-I) FOLKMAN M J; (WEIS-I) WEISZ P B; (CHIL-N) CHILDERN HOSPITAL
COUNTRY COUNT:	20

PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 325199	A	19890726	(198930)*	EN	9
R: AT BE CH DE ES FR GB GR IT LU NL SE					
ZA 8900383	A	19891025	(198947)		
JP 01279828	A	19891110	(198951)		
JP 03502323	W	19900530	(199128)		
US 5135919	A	19920804	(199234)		6
IL 88970	A	19930513	(199324)		
EP 398925	B1	19931020	(199342)	EN	12
R: AT BE CH DE FR GB IT LI LU NL SE					
EP 325199	B1	19931027	(199343)	EN	11
R: AT BE CH DE ES FR GB GR IT LI LU NL SE					
DE 68910113	E	19931125	(199348)		
DE 68910138	E	19931202	(199349)		

CA 1330943	C	19940726 (199432)	
ES 2059571	T3	19941116 (199501)	
CA 1333363	C	19941206 (199504)	
IE 64346	B	19950728 (199538)	
JP 2806454	B2	19980930 (199844)	6
KR 128287	B1	19980402 (200009)	

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
EP 325199	A		EP 1989-100714	19890117
ZA 8900383	A		ZA 1989-383	19890117
JP 01279828	A		JP 1989-5968	19890117
JP 03502323	W		JP 1989-501676	19890117
US 5135919	A	CIP of	US 1988-145407	19880119
			US 1988-173305	19880325
IL 88970	A		IL 1989-88970	19890117
EP 398925	B1		EP 1989-901794	19890117
			WO 1989-US175	19890117
EP 325199	B1		EP 1989-100714	19890117
DE 68910113	E		DE 1989-610113	19890117
			EP 1989-901794	19890117
			WO 1989-US175	19890117
DE 68910138	E		DE 1989-610138	19890117
			EP 1989-100714	19890117
CA 1330943	C		CA 1989-588421	19890117
ES 2059571	T3		EP 1989-100714	19890117
CA 1333363	C		CA 1989-588398	19890117
IE 64346	B		IE 1989-125	19890117
JP 2806454	B2		JP 1989-5968	19890117
KR 128287	B1		KR 1989-441	19890117

FILING DETAILS:

PATENT NO	KIND		PATENT NO
EP 398925	B1	Based on	WO 8906536
DE 68910113	E	Based on	EP 398925
		Based on	WO 8906536
DE 68910138	E	Based on	EP 325199
ES 2059571	T3	Based on	EP 325199
JP 2806454	B2	Previous Publ.	JP 01279828

PRIORITY APPLN. INFO: US 1988-173305 19880325; US 1988-145407 19880119; US 1989-295638 19890110

AB EP 325199 A UPAB: 20000218

Use of fumagillin (I) or salt is claimed for prepn. of a compsn. for treating or preventing angiogenesis, pref. together with an agent which potentiates the inhibition of angiogenesis. Compsns. comprising (I) and potentiator are also claimed. (I) is known from e.g. US2803586.

USE - Useful in treatment of diabetic retinopathy, trachoma, retrolental fibroplasia, corneal graft revascularisation, neovascular glaucoma, ocular tumours; psoriasis, pyogenic granuloma; juvenile haemangioma, angiofibroma and haemophiliac joints; hypertrophic scars, wound granulation, vascular adhesions, rheumatoid arthritis, scleroderma and atherosclerotic plaque. Doses are 1-200, pref. 2-100 mg/kg/day, p.o.; 0.1-20, pref. 0.2-10 mg/kg/day parenterally, pref. as Na salt; or for topical use, e.g. eye-drops contg. 0.001-3% w/v.

Dwg.0/1

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